AUTOMATIC ASSEMBLY OF SKELETON STRUCTURES. 3.* STEREOSELECTIVE SYNTHESIS, STEREOCHEMISTRY, AND CYCLIZATION OF *d,l*-α,α′-DIOXY-α,α′-DI-*tert*-BUTYLGLUTARIC ACID

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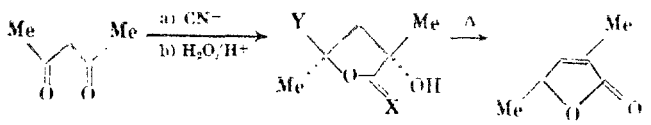
Stereoselective synthesis of d,l-α,α′-*dioxy*-α,α′-*di*-tert-*butylglutaric acid hydroxyiminolactonitrile (3) was conducted by the reaction of dipivaloylmethane with HCN in ether. The corresponding hydroxylacetonitrile (4) and amide (5), acid (6), and its ester (7), from which dilactone (8) was synthesized with preparative yields, were obtained from 3. Benzyl amide (9) was obtained by the reaction of 8 with* $BnNH_2$. *The iminolactone structure 3 of dipivaloylmethane bis-cyanohyrin, the* cis-*pseudo-*a *orientation of the functional substituents in 3-7 and 9, and the structure of the dilactone 8 were confirmed by the* ^1H, ^{13}C *NMR, IR and mass spectra.*

Keywords: *stereoselective synthesis, stereochemistry, cyclization, γ-lactone,* ^1H *and* ^{13}C *NMR, mass spectra.*

According to the principle of stereocontrolled cyclization [2, 3], the formation of dilactones from α,α′-dioxy-α,α′-dialkylglutaric acids is only possible from *d,l*-forms, since the functional groups have a *trans* orientation in meso forms of monolactones.

Iminolactonitriles of the meso form alone or mixtures of meso and *d,l*-α,α′-dioxy-α,α′-dialkylglutaric acids have been prepared by cyanohydrination of 1,3-diketones [3, 4], making preparative synthesis of dilactones impossible. **A** and **B** — meso-α,α′-dioxy-α,α′-dimethylglutaric acid (DDG) derivatives — were subsequently prepared from acetylacetone (AA). **B** is subsequently cyclized with a yield of ~20% only after epimerization in conditions of thermolysis: unsaturated lactone **C** is basically formed [3].



We found that cyanohydrination of dipivaloylmethane (DPM) yields cyclic derivatives exclusively of the *d,l*-form of α,α′-dioxy-α,α′-di-*tert*-butylglutaric acid (DBG), where the *cis*-pseudo-*a*-orientation of the functional substituents, which favors repeated cyclization, allows obtaining *d,l*-DBG dilactone in soft conditions and with a high yield.†

DPM was obtained by the reaction of pinacolin with pivaloyl chloride in the presence of $NaNH_2$ with the method in [6] with a yield of ~40% (cf. [6, 7]) together with a by-product, the previously undescribed pivalimide (**1**) (yield of ~10%). DPM in the enol form was identified with the IR and PMR spectra with the spectra in [8].

In contrast to other 1,3-diketones [3, 4], it is not possible to conduct cyanohydrination of DPM in an aqueous medium. For this reason, the reaction of DPM with HCN was conducted in ether in the presence of Et_3N.

DPM monocyanohydrin (**2**) was obtained with a yield of ~35% in conditions of high dilution with a molar ratio of DPM:HCN = 1:6. In prolonged holding (20 days) of DPM with acetone cyanohydrin in ether at 20°C, a ratio of DPM:**2** ≈ 1:1 is established, which corresponds to the reversible character of the cyanohydrination reaction [9].

*For previous communication, see [2].

†For the first communication, see [5].

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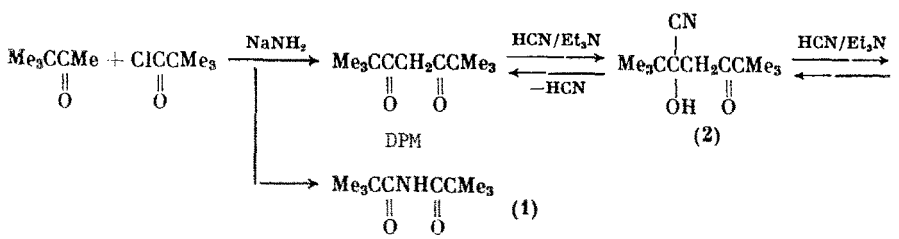
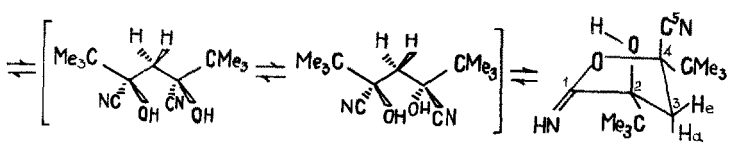
TABLE 1. Parameters of the PMR Spectra of 2-7 (δ, ppm, *J*, Hz)

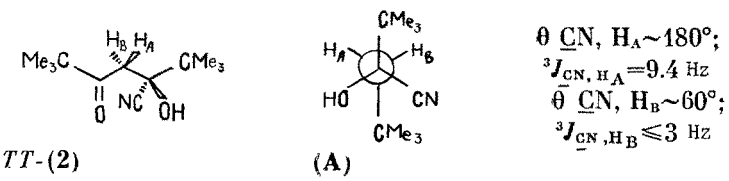
Compound	Solvent	δ					$^2J_{AB}$	$^4J_{H_B,OH}$
		Me_3C[a]	H_A	H_B	OH	Others[b]		
2	CD_3OD	1.09[c]	1.17	2.79 d[c]	3.17 d	–	–	−17.5	–
	$CDCl_3$	1.11	1.21[c]	2.52 d	3.22 d	5.56 s		−17.3	–
	C_6D_6	0.80	0.96	2.03 d	2.88 d	5.89 s	–	−17.1	–
3	DMSO-d_6	1.02	1.02	2.10 d	2.52 d.d	5.53 d	8.32 s	−14.4	1.1
	CD_3OD	1.10	1.10	2.22 d	2.62 d	–	–	−14.4	–
	$CDCl_3$	1.120	1.125[c]	2.30 d	2.49 d.d	2.42 d	7.45 s	−14.2	2.2
	C_5D_5N	1.09	1.36[c]	2.57 d	2.69 d[c]	–	5.01 s	−13.9	≤1.0
	C_6D_6	0.80	0.95[c]	2.01 d	2.01 d	2.10 t	7.21 s	–	1.2
4	CD_3OD	1.06[c]	1.12	2.30 d	2.67 d	–	–	−14.5	–
	$CDCl_3$	1.10[c]	1.15	2.36 d	2.53 d.d	2.56 d	–	−14.1	2.3
	C_6D_6	0.73	0.76	1.90 d	1.94 d[c]	2.08 s[c]	–	−14.2	≤1.0
5	DMF-d-	0.94	0.96	2.53 s	2.53 s	5.47 s	7.16 s 7.24 s	–	–
	CD_3OD	1.05	1.06[c]	2.46 s	2.46 s	–	–	–	–
	$CDCl_3$	1.06	1.09[c]	2.41 d[c]	2.60 d	2.18 s[c]	5.64 s[c] 6.37 s[c]	−14.3	≤1.0
	C_6D_6	0.93	0.94	2.17 d[c]	2.64[d]	–	5.11 s 5.75 s	−14.2	≤1.0
6	D_2O	0.82	0.82	2.23 d	2.45 d	–	–	−14.7	–
	CD_3OD	1.05	1.05	2.40 d	2.50 d	–	–	−13.9	–
	$CDCl_3$	1.08	1.09	2.43 d	2.49 d	–	–	−14.2	–
	C_6D_6	0.93	0.95	2.18 d	2.50 d	–	–	−14.1	–
7	CD_3OD	1.01	1.04	2.36 d	2.50 d	–	3.73 s	−14.1	–
	$CDCl_3$	1.04	1.08[a]	2.40 d.d	2.46 d	2.22 d	3.73 s	−14.2	2.0
	C_6D_6	0.88[c]	0.93	2.14 d.d	2.43 d	1.80 d	3.40 s	−13.9	2.3
	$C_6D_5CD_3$	0.86[c]	0.91	2.12 d[c]	2.37 d	1.85 s[c]	3.42 s	−13.7	≤1.0

Notes. a) Singlet. b) NH (**3**, **5**), OMe (**7**). c) Signal is broadened.





According to the NMR data, the *TT*-conformer significantly predominates in **2**: the $^3J_{CH}$ SSCC of the CN group carbon with protons H_A and H_B correspond to dihedral angles at the projection of **A** and correlated with the $^3J_{CN,H_A(H_B)}$ SSCC in **3**, **4** (see below) based on $^3J_{CH} = f(\theta)$ [10].



The product of the second stage of cyanohydrination of DPM (in concentrated solution with a molar ratio of DMP:HCN = 1:12) — DPM biscyanohydrin (BCH), similar to the derivatives of AA and propionyl acetone in [3] — is spontaneously cyclized into *d,l*-BCH iminolactonitrile (**3**) with a 78% yield due to intramolecular nucleophilic addition at the CN group [11]. However, a significant difference from [3] is observed in our case. Due to the strong pseudo-*e*-preference of the *t*-Bu groups, only the *d,l*-form of BCH is cyclized, and the *TT*-conformer probably dominates in it (cf. [1]). *cis*-Isomer **3**, which has a pseudo-*a*-orientation of the functional groups, is exclusively formed.

TABLE 2. Parameters of the ^{13}C NMR Spectra of 3-7[a,b] (δ, ppm, J, Hz)

Parameter		Compound 3	4	5	6	7[c]
$\underline{Me_3C}$	δ	24.05[d]	24.31	25.00	24.90	24.38
	^1J	127.0	125.7	126.2	126.4	125.7
	^3J	4.9	4.4	4.9	4.3	4.7
	δ	24.55*[e]	24.76	25.58	25.34	24.93
	^1J	125.7	125.7	126.2	126.4	126.4
	^3J	–	4.4	4.9	4.3	4.7
$\underline{CMe_3}$	δ	36.51*[e,f]	36.90 m	36.88 m	36.63 d*[g]	35.64 m
	$^3J_{H_a}$; $^3J_{H_e}$[g]	2.5; <0.5	–	–	1.4; <0.5	–
	δ	37.06 m[d,f]	38.29	37.41	37.00 d*[g]	36.45
	^2J	3.7	3.6	3.5	–	3.6
	$^3J_{H_a}$; $^3J_{H_e}$[g]	3.5; <0.5	–	–	3.5; <0.5	–
C^3	δ	40.02	39.74	38.32	39.03	38.00 [h]
	$^1J^i_{H_a}$	131.2	131.5	131.1	129.0	129.3
	$^1J^i_{H_e}$	138.6	139.5	136.6	138.0	139.5
C^2	δ	81.25*[j]	81.50 m	81.79 m	81.72 d*[g]	80.96 m[k]
	^2J[g]	3.5; 4.2	–	–	5.6; <0.5	–
C^4	δ	82.65 m[j]	82.73 m	89.98 m	89.40 d.d[g]	88.43 m
	^3J	4.3	4.4	–	–	3.6
	^2J_g	1.4; 4.2	–	–	1.4; 4.9	–
C^5	δ	118.87	119.59	176.60	174.90	172.41 [l]
	$^3J_{H_a}$; $^3J_{H_e}$	8.5; 4.3	8.7; 4.4	5.8; 4.2	6.9; 3.5	7.2; 3.6
C^1	δ	169.41*	174.65 d*	175.99 d.d	176.02 d *	174.20 d.d
	$^3J_{H_e}$; $^3J_{H_a}$	–; –	7.3; ≤1.0	6.2; 1.4	6.9; ≤1.0	7.3; 2.2

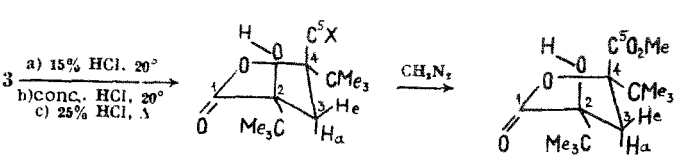
Notes. a) **3** in $CDCl_3$; **4-6** in CD_3OD; **7** in C_6D_6. b) **3,6** in "Gated" and in conditions of {CMe_3}. c) OMe: δ = 52.07 ppm; ^1J = 147.5 Hz. d) *t*-Bu group at the C^4 of the ring. e) *t*-Bu group at the C^2 of the ring. f) In conditions of {CMe_3}, the signal degenerates into a broadened doublet. g) Measured in conditions of {CMe_3}. h) $^3J_{\underline{OH}}$ = 5.8 Hz. i) $^1J_{CH}$ SSCC assigned with the signals of ^{13}C satellites and PMR spectra. j) In conditions of {CMe_3}, the signal degenerates into a doublet of doublets. k) ^3J = 3.6 Hz. l) $^3J_{\underline{OMe}}$ = 3.6 Hz.

*Signal is broadened.

The iminolactonitrile structure of **3** is confirmed by the spectral data. Nonequivalence of the *t*-Bu groups and methylene protons is observed according to PMR and nonequivalence of all C atoms (except for the Me of each *t*-Bu group) and the signals with chemical shifts characteristic of C=N and C≡N groups is observed with ^{13}C NMR. There is an intense band of C=N (C≡N is not detected; cf. [3]) in the IR spectrum.

In contrast to DDH derivatives [3], neither the open form — BCH, nor the mutual conversion of *cis* and *trans* isomers is observed with the PMR spectra of **3** in C_5D_5N and DMSO-d_6 (Table 1). In CD_3OD **3** is decyanohydrinated into DPM after 20 days. In addition, a significant proportion of **3** and the presence of DPM are observed when the reaction of DPM with HCN is conducted for a long time in solution together with **2**. This indicates the reversible character of both the first (see above) and the second stage of cyanohydrination of DPM. It should be emphasized that *cis* isomer **3** is exclusively observed during formation in preparation of DPM BCH both in solution and in conditions of precipitation. For this reason, we can hypothesize that the *d,l* form of **3** is thermodynamically and kinetically controlled by the production of cyanohydrination of DPM.

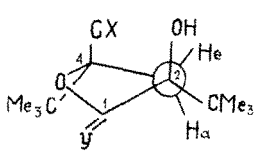
In thermolysis (170-180°C/atm), **3** decomposes into **2** with liberation of HCN_2, which corresponds to the thermal instability of cyanohydrins [11].



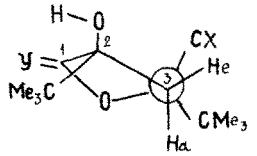
CX, a) CN (4), b) C(O)NH_2 (5), c) CO_2H (6) (7)

Compound **3** is easily hydrolyzed into lactonitrile (**4**) with a dilute solution of HCl (cf. [3]). Lactonamide (**5**) and lactonic acid (**6**) were obtained by subsequent hydrolysis. Treatment of **6** with CH_2N_2 yields lactonic ester (**7**). In contrast to **3**, the IR spectra of **4-7** have a band of lactone C=O stretching vibrations in the 1778-1795 cm^{-1} region.

The *cis* configuration of **3-7**, the pseudo-*a*-orientation of the functional substituents, and the almost envelope conformation of the γ-lactone ring were established with PMR (Table 1) and ^{13}C NMR spectra (Table 2). The following spectral parameters are key: a) pronounced SSCC $^4J_{HH}$ = 1.1-2.3 Hz (in some solvents, broadening of the signal) of the OH group proton (at C^2) with the H_a methylene proton (projection **B**); b) correspondence of the $^3J_{CH}$ SSCC of C^1, C^5 and $\underline{C}Me_3$ carbons with CH_2 group protons to the torsion angles in projections **B** and **C**.



Y=NH (**3**)
O (**4**)–(**7**)



(**B**) C^2-C^4
θ $\underline{C}X$, H_a~155°; θ $\underline{C}Me_3$, H_e~85°;
θ $\underline{C}X$, H_e~θ $\underline{C}Me_3$, H_a~35°;

(**C**) C^5-C^1
θ C^1, H_e~155°; θ $\underline{C}Me_3$, H_a~35°;
θ C^1, H_a~θ $\underline{C}Me_3$, H_e~85°

The presence of the $^4J_{\underline{O}H,H_a}$ SSCC indicates the pseudo-*a*-orientation of the OH group, since only an almost coplanar *W* configuration of this fragment (projection **B**) is realized.

In contrast to **3-5** and **7**, the $^4J_{\underline{O}H,H_a}$ SSCC is not observed for lactonic acid **6**, probably because of the precipitation of the OH group (at C^2) in the association which brings the O—H bond out of a plane of the *W* type. Although the bands of stretching vibrations of free OH bonds are observed in the IR spectra ($CHCl_3$) of **3-5** and **7** at 3590 or 3595 cm^{-1} (and correspondingly $^4J_{\underline{O}H,H_a}$ with PMR), there is a broad band in the 3450-3600 cm^{-1} region for **6** which turns into individual narrow bands at 3575 and 3590 cm^{-1} on dilution. The participation of **6** in the intermolecular H bond is confirmed by the shift of carboxyl $\nu_{C=O}$ in **6** (1723 cm^{-1}) in the long-wave region in comparison to **7** (1742 cm^{-1}).

The signals of H_a and H_e protons in the PMR spectra were assigned based on the presence of $^4J_{\underline{O}H,H_a}$ SSCC or the broadening of the corresponding signals if the $^4J_{\underline{O}H,H_a}$ SSCC is not observed. In substitution of a CN group (at C^4) in **3, 4** by C(O)R (R = NH_2, OH, OMe) in **5-7**, the signals of these protons in the PMR spectra "change" places as a result of shielding of H_a and deshielding of H_e (Table 1).

Using *d,l*- and meso-α,α′-dioxyglutaric acid (DOG) [1] and DDG [3] monolactones, it was previously shown that $\Delta\nu_{AB}$ of the CH_2 protons of the ring is greater for the *cis* than for the *trans* isomer; this is one criterion for configurational assignment. However, in the derivatives of *d,l*-BDG **3-7**, the pseudo-*e*-oriented *t*-Bu substituents cause a paramagnetic shift of the strong-field H_A proton and a diamagnetic shift of the weak-field H_B (in comparison to the corresponding protons of *d,l*-DOG [1] and *d,l*-DDG monolactones [3]), causing an important decrease in $|\Delta\nu_{AB}|$ and as a result impedes the configurational assignment of **3-7** based on this trait (Table 1).

In the ^{13}C NMR spectra (Table 2, the $^3J_{CH}$ SSCC of the C^5 carbon with CH_2 group protons in **3** and **4** ($^3J_{CN,H_a}$ = 8.5 and 8.7; $^3J_{CN,H_e}$ = 4.3 and 4.4 Hz) and **5-7** ($^3J_{\underline{C}(O)R,H_a}$ = 5.8-7.2, $^3J_{\underline{C}(O)R,H_e}$ = 3.5-4.2 Hz) correspond to exocyclic torsion angles of $\theta \sim 155$ and $\sim 35°$ (projection **B**) (cf. [12]). This indicates the pseudo-*a*-orientation of the functional group at C^4. In addition, the value of $^3J_{\underline{C}X,H}$ is correlated with the corresponding SSCC of derivatives of *d,l*-DOG [1] and *d,l*-DDG [3].

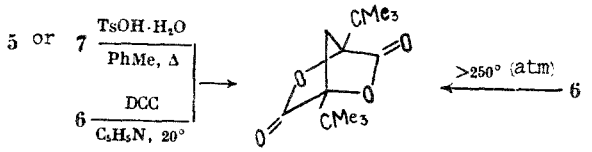
The pseudo-*e*-orientation of *t*-Bu groups at $C^{2,4}$ in **3** and **6** was confirmed as follows. In conditions of selective heteronuclear uncoupling from the {CMe_3} protons, the $^3J_{CH}$ SSCC of quaternary carbons of *t*-Bu groups with methylene protons ($^3J_{\underline{C}Me_3,H_a}$ = 1.4-3.5; $^3J_{\underline{C}Me_3,He_e} < 0.5$ Hz) correspond to dihedral angles of $\theta \sim 35$ and $\sim 85°$ (projections **B, C**) (cf. [12]). The $^3J_{CH}$ SSCC of the C=O carbons in the ring of **4-7** with the protons of the CH_2 group ($^2J_{C^1,H_e}$ = 6.2-7.3 Hz; $^3J_{C^1,H_a} \simeq$ 1.0-2.2 Hz) correspond to $\theta \sim 155$ and $\sim 85°$ (projection **C**), which indicates the close-to-envelope conformation of the γ-lactone ring.

In the ^{13}C NMR spectrum of **3**, the signals of C^2 and the *t*-Bu group bound with it were assigned based on their broadening, preferably due to hindered rotation of the *t*-Bu group and/or quadrupole broadening at the ^{14}N of the imino group. The signals of $C^{2,4}$ were subsequently assigned to the spectra of **4-7** by comparison of the chemical shifts with **3**.

The structure, configuration, and conformation of *d,l*-BDG derivatives was thus unambiguously established based on these data.

The *cis*- and pseudo-*a*-orientation of the functional substituents in **5-7** allow obtaining *d,l*-BDG dilactone **8** in soft conditions and with a high yield: a) from lactonamide **5** and lactonic ester **7** with $TsOH \cdot H_2O$ in toluene with a yield of ~85 and ~65%,

respectively; b) from lactonic acid **6** with dicyclohexylcarbodiimide (DCC) in C_5H_5N, yield of ~100% (PMR). In addition, in thermolysis of **6**, dilactone **8** was obtained with an 80-85% yield (PMR):

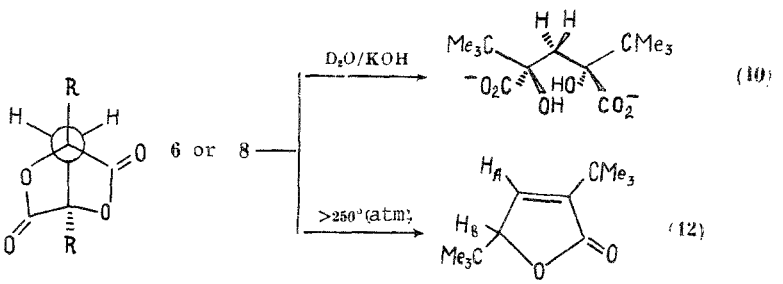


(8)

In contrast to [3], attempts to cyclize **3** or **4** in the conditions of the Pinner reaction did not cause the formation of BDG diimino- or corresponding iminolactone hydrochlorides.

According to the ^1H and ^{13}C NMR spectra of *d,l*-BDG (**8**) and *d,l*-DDG (**9**) dilactones (see Experimental), paired equivalence of the atoms in the skeletal structures corresponding to their C_2 symmetry of the norbornane type is observed [13]. It should be noted that the same SSCC with methylene protons, $^3J_{CH}$ = 4.6 Hz, are observed for carbonyl carbons due to the C_2 symmetry of the bicycle, and the SSCC with these protons are abnormally small for $\underline{C}Me_3$ **8** and Me **9** carbons: $^3J_{CH}$ < 2 Hz (projection **D**).

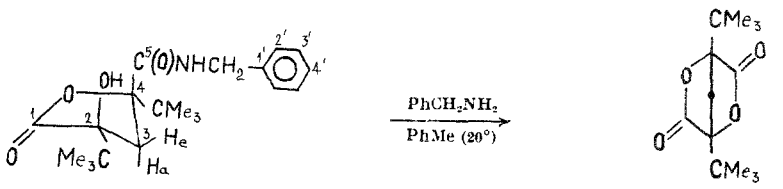
The products of basic hydrolysis of dilactone **8** and lactonic acid **6** were identified with the *d,l*-BDG salt (**10**) (the singlets of *t*-Bu and CH_2 groups at 0.65 and 2.14 ppm in the PMR spectra). This independently confirmed the *d,l*-configuration of **6**. In D_2O/KOH, **6** is totally converted into **10** after 10 h at 20°C (PMR), while **8** is only converted on boiling for 7 h (PMR does not show the formation of **10** after 3 days at 20°C). For comparison, we note that *d,l*-DDG dilactone **9** is totally converted into *d,l*-DDG *cis*-lactonic acid when heated in H_2O for 5-10 min, and after 2 days at 20°C [4] (the *d,l*-DDG salt is observed with the PMR spectrum only in D_2O/KOH [3]). The difficult hydrolysis of **8** in comparison to **9** is not only due to the poor solubility of **8** in H_2O but also due to the greater (+*I*) effect and the steric character of the bulky *t*-Bu substituents which prevent attack of the nucleophile at the dilactone C=O groups.



(**D**) R=CMe_3 (**8**), Me (**9**)

For example, the reaction of dilactone **8** with $BnNH_2$ in the molar ratio of 1:4 in toluene at 20°C takes place with opening of only one γ-lactone ring and the formation of benzyl amide (**11**). The bulky substituent at C^4 probably additionally shields the C=O group of **11**, preventing further reaction of Ad_N. After boiling **11** with $BnNH_2$ in toluene-d_8 for 5 h, dibenzyl amide was not recorded (PMR). The reverse reaction — cyclization of **11** into **8** by TsOH·H_2O while boiling in toluene takes place in more rigorous conditions and with a lower yield (~72%) in comparison to **5**.

The stereochemistry of **11**, similar to **3-7**, is confirmed by the $^3J_{CH}$ SSCC of the C^1 and C(O)NH carbons with the CH_2 group protons of the ring.



(**8**) (**11**)

In distillation with heating on the open flame of a burner at atmospheric pressure, dilactone **8** is partially decarboxylated with a 1,2-shift of H and forms α,γ-di-*tert*-butyl-γ-crotonolactone (**12**) (~15%), while **9** is distilled without decomposition in these conditions [4]. The signals in the PMR spectrum of **12** were assigned by analogy with γ-crotonolactones in [1, 3].

EXPERIMENTAL

The IR spectra were made on a UR-20 spectrophotometer in $CHCl_3$, the NMR spectra were made on a Bruker WM-400 spectrometer (^1H 400.13; ^{13}C 100.62 MHz) vs. TMS internal standard (δ, ppm, J, Hz), and the mass spectra were recorded on a Hitachi M-80A mass spectrometer at 20 eV (the peaks with a relative intensity $>10\%$ are reported). The samples of **1-4** were crystallized with natural evaporation of the solvents; petroleum ether was used with bp 40-70°C. The melting points were determined on a Boetius RNMK-05 stage. The PMR and ^{13}C NMR spectra of **3-7** are reported in Tables 1 and 2.

Pivaloyl Chloride. Using method **B** [6], 36.4 g (88%) was obtained from a mixture of 35 g (0.34 mole) of pivalic acid and 72.3 g (59.7 ml, 0.51 mole) of benzoyl chloride. PMR spectrum (C_6D_6): 0.89 s (Me_3C).

Dipivaloylmethane (DPM). Pivalimide (1). A solution of 50 g (0.5 mole) of pinacolin [PMR spectrum (C_6D_6): 0.88 s (Me_3C, 9H); 1.73 s (MeCO, 3H)] in 50 ml of ether was added by drops over 15 min while stirring at 20°C to a suspension of sodium amide (0.5 mole) in 200 ml absolute ether (prepared according to [7] from 12.8 g (~10% excess) of sodium and 300 ml of ammonia). The color of the mixture changed from dark grey to black, and 200 ml of ether was added after it was vacuum-evaporated at 20-25°C (~150 ml). While stirring, a solution of 30.2 g (0.25 mole) of pivaloyl chloride in 50 ml of ether was added over 10 min at 20°C. The color changed to yellow-green. It was stirred for another 1 h at 20°C and 2 h at 35°C, cooled to ~5°C, and poured in 300 ml of ice water. A 5% solution of HCl was added to pH 1 and extracted with ether (3 × 200 ml). The ether solution was washed with concentrated $NaHCO_3$ solution, dried over $MgSO_4$, filtered, and vacuum-evaporated. The sediment was distilled, collecting the fraction with bp 85-100°C (20 mm Hg). The sediment formed after some time was filtered off and washed with petroleum ether. After three distillations with a fractionating column, 18.5 g (40.1%) DPM was obtained, a colorless liquid with bp 56-58°C (3 mm Hg), freely soluble in ether and petroleum ether. PMR spectrum ($CDCl_3$): 1.18 s (Me_3C, 18H), 5.73 s (CH=C, 1H). IR spectrum (ν, cm^{-1}): 1600 (C=C—C=O), 3590 (OH).

The sediment was recrystallized from ether, then from benzene, yielding 4.5 g (9.7%) of **1**; long white crystals with mp 80-82°C, freely soluble in acetone, $CHCl_3$, sparingly soluble in ether and benzene, and difficultly soluble in petroleum ether. Found, %: C 64.83; H 10.38; N 7.81. $C_{10}H_{19}NO_2$. Calculated, %: C 64.83; H 10.34; N 7.56. IR spectrum (ν, cm^{-1}): 1595, 1680, 1764 (C=O), 3425, 3475, 3545. PMR spectrum ($CDCl_3$): 1.26 s (Me_3C, 18H), 8.29 s (NH, 1H). ^{13}C NMR spectrum ($CDCl_3$): 27.01 ($\underline{Me}_3C$, ^1J = 127.6, ^3J = 4.2), 40.64 m ($\underline{C}Me_3$, ^2J = 4.2), 175.62 m (C=O, ^3J = 4.2). Mass spectrum (12 eV), *m/z* (I_{rel}, %): $[M + H]^+$ 186(3.9), M^+ 185(10.2), 130(11.2), 102(14.1), 101(11.7), 86(11.7), 85(18.0), 57(100).

Dipivaloylmethane Monocyanohydrin (2). a. A mixture of 1.84 g (10 mmoles) of DPM, 1.62 g (60 mmoles) of HCN (prepared according to [14]), and 51 mg (0.05 mmole) of absolute Et_3N in 100 ml of absolute ether was held for 5 days at 20°C, the solution was then evaporated dry in a vacuum, and the solid sediment was washed with 100 ml of petroleum ether at 0°C (**3**, mp 170-175°C; see below). The filtrate was evaporated dry in a high vacuum at 20°C. The crystallized part was washed with cold petroleum ether (0°C) one day later to remove the oil and recrystallized from ether, yielding 0.74 g (35.1%) of **2**, white crystals with mp 66°C, freely soluble (but less than DPM) in $CHCl_3$, benzene, and petroleum ether. Found, %: C 68.21; H 10.28; N 6.62. $C_{12}H_{21}NO_2$. Calculated, %: C 68.21; H 10.02; N 6.63. IR spectrum (ν, cm^{-1}): 1700 (C=O), 3300-3600 (OH). The PMR spectra are reported in Table 1. ^{13}C NMR spectrum ($CDCl_3$): 24.53 ($\underline{Me}_3C$, ^1J = 126.4, ^3J = 4.4), 25.83 ($\underline{Me}_3C$, ^1J = 127.2, ^3J = 4.4), 37.87 br.m [$Me_3\underline{C}C(OH)$], 39.16 d.t (CH_2, ^1J = 127.9, $^3J_{\underline{OH}}$ = 1.5), 45.14 m ($Me_3\underline{C}CO$, ^2J = 3.6), 75.96 m ($\underline{C}$—OH), 120.56 br.d (C≡N, $^3J_{H_A}$ = 9.4, $^3J_{H_B} \leq 3.0$), 217.47 m (C=O, ^3J = 4.0). Mass spectrum, *m/z* (I_{rel}, %): M^+ 211(0.5), 127 (27.2), 100(23.3), 85(16.0), 57(100).

b. Here 1.22 g (14.4 mmoles) of acetone cyanohydrin was added to a solution of 0.33 g (1.8 mmoles) of DPM and 0.14 g (1.4 mmoles) of Et_3N in 20 ml of absolute ether and held for 20 days at 20°C. According to the PMR spectrum, DPM:**2** ≈ 1:1.

***cis*-2-Hydroxy-2-cyano-2,4-di-*tert*-butyl-γ-iminobutyrolactone (3).** A mixture of 9.21 g (50 mmoles) of DPM, 16.21 g (0.6 mole) of HCN, and 0.51 g (5 mmoles) of absolute Et_3N in 50 ml of absolute ether was held for 5 days at 20°C and the mixture and sediment was then evaporated dry in a vacuum at 20°C. The dark brown residue was washed with 50 ml of petroleum ether and extracted with hot benzene (60-70°C). The extract was filtered, evaporated dry in a vacuum, and the residue was recrystallized from ether, yielding 9.29 g (78%) of **3**, a white powder with mp 175-177°C (with decomposition), freely soluble (but less than **2**) in $CHCl_3$, ether, hot benzene, and sparingly soluble in cold benzene, petroleum ether, and H_2O. Sublimation at 130-140°C (10-15 mm Hg) yielded an analytical sample of **3** with mp 177°C (with decomposition). Found, %: C 65.56; H 9.45; N 11.49. $C_{13}H_{22}N_2O_2$. Calculated, %: C 65.51; H 9.31; N 11.75. IR spectrum (ν, cm^{-1}): 1702 (C=N in ring), 3300 (NH), 3595 (OH). Mass spectrum, *m/z* (I_{rel}, %): $[M + H]^+$ 239(1.0), 182(49.5), 137(16.0), 110(100), 88(14.1), 57(46.6), 18(18.4).

***cis*-2-Hydroxy-4-cyano-2,4-di-*tert*-butyl-γ-butyrolactone (4).** Here 30 ml of 15% HCl solution was added to 476 mg (2 mmoles) of **3** and the mixture was held for 24 h at 20°C. The substance dissolved after approximately 1 h, and a sediment

then precipitated out of the solution. The mixture was extracted with ether (4 × 20 ml), the extract was dried over $MgSO_4$ and filtered, evaporated dry in a vacuum at 20°C, and the residue was recrystallized from ether, yielding 405 mg (84%) of **4**, a white powder with mp 151-153°C freely soluble in $CHCl_3$ and difficultly soluble in H_2O. Sublimation at 120-130°C (10-15 mm) yielded an analytical sample of **4** with mp 153°C. Found, %: C 65.27; H 8.77; N 6.06. $C_{13}H_{21}NO_3$. Calculated, %: C 65.25; H 8.85; N 5.85. IR spectrum (ν, cm^{-1}): 1795 (C=O in ring), 3595 (OH). Mass spectrum, *m/z* (I_{rel}, %): 183(20.4), 110(67.0), 96(27.2), 95(9.7), 57(100).

2-Hydroxy-2,4-di-*tert*-butyl-γ-butyrolactone-4-carboxylic Acid *cis*-Amide (5). Here 200 ml of concentrated HCl was poured in 2.38 g (10 mmoles) of **3**, the mixture was held for 10 days at 20°C, extracted with hot benzene (60-70°C, 5 × 200 ml), the extract was dried over $MgSO_4$, filtered, and evaporated dry in a vacuum at 20°C. The residue was recrystallized from benzene yielding 208 mg (81%) of **5**, a white powder with mp 227-229°C. Sublimation at 150-160°C (2 mm Hg) produced an analytical sample with mp 229°C. Found, %: C 60.68; H 9.05; N 5.62. $C_{13}H_{23}NO_4$. Calculated, %: C 60.68; H 9.01; N 5.44. IR spectrum (ν, cm^{-1}): 1484, 1580 (δ, NH, amide-II), 1700 (C=O, amide-I), 1782 (C=O in ring), 3420 and 3540 (NH), 3590 (OH). Mass spectrum, *m/z* (I_{rel}, %): $[M - H]^+$ 256(1.2), 213(11.1), 186(11.1) 185(84.6), 128(43.3), 113(20.3), 110(12.1), 88(17.0), 85(42.3), 57(100).

***cis*-2-Hydroxy-2,4-di-*tert*-butyl-γ-butyrolactone-4-carboxylic Acid (6).** Here 450 ml of a 25% solution of HCl was added to 4.76 g (20 mmoles) of **3** and the mixture was held for 1 h at 20°C, then boiled for 6 h. After cooling, 250 ml of H_2O was poured in and the mixture was extracted with ether (10 × 200 ml), the ether extract was dried over $MgSO_4$, filtered, and evaporated dry in a vacuum at 20°C. The oily residue was recrystallized from benzene, yielding 4.38 g (85%) of **6**, a white powder with mp 195-198°C, freely soluble in DMSO, MeOH, ether, $CHCl_3$, and hot benzene and sparingly soluble in acetone and cold benzene. Sublimation at 145-155°C (1 mm) produced an analytical sample of **6** with mp 198°C. Found, %: C 60.49; H 8.58. $C_{13}H_{22}O_5$. Calculated, %: C 60.49; H 8.52. IR spectrum (ν, cm^{-1}): 1723 (CO_2H), 1778 (C=O in ring), 3450-3600 (OH) (on dilution changes into separate bands: 3575 and 3590). Mass spectrum, *m/z* (I_{rel}, %): 202(36.9), 196(9.7), 185(44.7), 181(11.7), 174(10.7), 129(23.3), 115(15.0), 114(58.3), 111(31.1), 86(13.1), 85(30.1), 57(100).

***cis*-2-Hydroxy-4-methoxycarbonyl-2,4-di-*tert*-butyl-γ-butyrolactone (7).** A solution of 516 mg (2 mmoles) of **6** in 200 ml of absolute ether was treated with an ether solution of CH_2N_2 then filtered and evaporated dry in a vacuum at 20°C. The residue was recrystallized from petroleum ether, yielding 474 mg (87.1%) of **7**, transparent colorless crystals with mp 124°C, freely soluble in ether, $CHCl_3$, benzene, and sparingly soluble in MeOH and petroleum ether. Found, %: C 61.74, H 8.77. $C_{14}H_{24}O_5$. Calculated, %: C 61.74; H 8.88. IR spectrum (ν, cm^{-1}): 1742 (CO_2Me), 1780 (C=O in ring), 3595 (OH). Mass spectrum, *m/z* (I_{rel}, %): $[M + H]^+$ 273(0.2), 216(15.4), 196(18.3), 185(57.7), 181(12.5), 143(21.2), 129(9.6), 128(32.7), 111(26.0), 96(11.1), 85(32.7), 57(100).

***d,l*-Form of *a,a'*-Dioxy-*a,a'*-di-*tert*-butylglutaric Acid Dilactone (8). a. Cyclization of 5 with $TsOH \cdot H_2O$.** Here 1.05 g (5.5 mmoles, 10% excess) of $TsOH \cdot H_2O$ was added to a boiling solution of 1.29 g (5 mmoles) of **5** in 300 ml of absolute toluene and boiled for 1 h. It was then cooled to 20°C, filtered, and the sediment was washed with benzene (50 ml). The combined filtrate was evaporated dry in a vacuum at 20°C. The brown crystalline residue was washed with H_2O to pH 7, dried in a high vacuum at 20°C, and sublimated at 120-130°C (10-15 mm), yielding 1.02 g (84.6%) of **8**, a white powder (flakes under the microscope) with mp 172-174°C (with decomposition), freely soluble in $CHCl_3$, sparingly soluble in ether and benzene, and difficultly soluble in MeOH and hot H_2O. Found, %: C 64.98; H 8.36. $C_{13}H_{20}O_4$. Calculated, %: C 64.98; H 8.39. IR spectrum (ν, cm^{-1}): 1800 (C=O). PMR spectrum ($CDCl_3$): 1.19 s (Me_3C, 18H), 2.37 s (CH_2, 2H). ^{13}C NMR spectrum ($CDCl_3$) (in conditions of {Me_3C}): 24.48 ($\underline{Me}_3C$, ^1J = 126.9, ^3J = 4.9), 31.50 ($\underline{C}Me_3$, ^2J = 4.2) [br.s, ^3J < 1.5], 43.20 t (CH_2, ^1J = 138.1), 91.44 m ($\underline{C}$—C=O) [t, $^5J_{\underline{CH_2}}$ = 1.7], 169.25 t (C=O, $^3J_{\underline{CH_2}}$ = 4.6) [s, in conditions of {CH_2}]. Mass spectrum, *m/z* (I_{rel}, %): 196(15.1), 181(25.2), 140(10.2), 111(100), 85(13.1), 83(44.7), 57(75.7), 55(18.9), 41(8.3).

b. Cyclization of 7 with $TsOH \cdot H_2O$. A mixture of 350 mg (1.29 mmoles) of **7** and 490 mg (2.58 mmoles, 100% excess) of $TsOH \cdot H_2O$ in 70 ml of absolute toluene was boiled for 10 h with a Dean—Stark trap, cooled to 20°C, and the precipitated sediment was filtered off after 1 h and washed with benzene (20 ml). The combined filtrate was evaporated dry in a vacuum at 20°C. The dark brown residue was washed with H_2O to pH 7, dried in a high vacuum at 20°C, and sublimated at 120-130°C (10-15 mm Hg), yielding 0.2 g (64.7%) of **8**; it was identified by the mp and PMR spectrum.

c. Cyclization of 6. *1. With DCC.* A solution of 43 mg (0.21 mmole, ~10% excess) of DCC in 5 ml C_5H_5N was added by drops to a solution of 50 mg (0.19 mmole) of **6** in 5 ml of absolute C_5H_5N and stirred at 20°C. Sediment precipitated during the 1 h of the reaction, there was no **6** in the reaction mixture after 6 h, and **8** was formed with ~100% yield (according to PMR). *2. In conditions of thermolysis.* Here 0.1 g of **6** was slowly melted over the open flame of a burner (atm.) and heated until liberation of gas stopped and the substance had totally evaporated from the still. The solid, almost colorless product in the container contained ~80-85% **8** and ~15% **12** (according to PMR).

^{13}C NMR spectrum (obtained from meso-DDG according to [4] with ~20% yield; (see [3]) ($CDCl_3$) [in conditions of {Me}]: 13.18 q (Me, ^1J = 130.1, $^3J_{CH_2}$ < 2.0), 51.34 t. sept (CH_2, ^1J = 140.1, $^3J_{Me}$ = 3.6) [t], 85.42 t.q (C—C=O, $^2J_{Me}$ = 5.1) [t, $^2J_{CH_2}$ = 1.3], 170.85 t.q (C=O, $^3J_{Me}$ = 4.5) [t, $^3J_{CH_2}$ = 4.6]. Mass spectrum, *m/z* (I_{rel}, %): 112(31.1), 69(100), 43(76.7), 41(64.6).

2-Hydroxy-2,4-di-*tert*-butyl-γ-butyrolactone-4-carboxylic Acid *cis*-Benzamide (11). A solution of 200 mg (0.83 mmole) of **8** and 360 mg (3.36 mmoles) of benzyl amide in 60 ml of absolute toluene was held for 12 h at 20°C, then evaporated dry in a vacuum at 20°C and the residue was extracted with a cold (~0°C) mixture of 15 ml of 5% HCl solution and 45 ml of ether. The ether layer was dried over $MgSO_4$, filtered, and evaporated dry in a vacuum of 20°C. The solid residue was recrystallized twice from benzene–petroleum ether mixture, yielding 226 mg (78.2%) of **11**, long white crystals with mp 162°C, freely soluble in benzene, $CHCl_3$ and ether, and sparingly soluble in petroleum ether. Found, %: C 69.22; H 8.34; N 4.13. $C_{20}H_{29}NO_4$. Calculated, %: C 69.14; H 8.41; N 4.03. IR spectrum (ν, cm^{-1}): 1434-1454, 1480, 1674 (C=O, amide-I), 1783 (C=O in ring), 3300-3390, 3452 (NH), 3586 (OH). PMR spectrum (C_6D_6): 0.92 br.s and 0.94 s (Me_3C, 18H), 2.23 d (H_A, 1H, $^2J_{AB}$ = −14.2), 2.73 d (H_B, 1H), 4.12 d.d and 4.22 d.d (CH_2Ph, 2H, $^2J_{A'B'}$ = −14.9, $^3J_{NH}$ = 6.1), 6.52 br.t (NH, 1H), 7.01, 7.09, and 7.16 (Ph, 5H). ^{13}C NMR spectrum (CD_3OD): 25.05 and 25.56 (Me_3C, ^1J = 126.2, ^3J = 4.2), 36.88 m (CMe_3), 38.01 m (CMe_3, ^2J = 4.2), 38.34 d.d (C^3, ^1J = 129.7 and 138.7), 44.17 t.t (C-Ph, ^1J = 138.0, ^3J = 4.2), 81.74 m (C^2, ^3J = 4.3), 89.97 m (C^4), 128.37 d.t ($C^{4'}$, ^1J = 159.5, J = 7.2), 128.73 d.m ($C^{2'}$, ^1J = 157.0), 129.05 d.d ($C^{3'}$, ^1J = 159.1, J = 7.8), 139.79 m ($C^{1'}$), 173.69 m [C(O)NH, $^3J_{H_a}$ = 6.9, J = 3.5 and 2.8), 176.03 br.d (C=O in ring, $^3J_{H_e}$ = 6.9, $^3J_{H_a} \leq 1.0$]. Mass spectrum, *m/z* (I_{rel}, %): M + H]$^+$ 348(9.9), M$^+$ 347(51.7), 218(26.2), 186(11.0), 185(100), 111(10.9), 106(18.2), 91(12.8), 85(48.4), 57(62.8).

Cyclization of 11 with $TsOH \cdot H_2O$. Here 185 mg (0.97 mmole, 200% excess) of $TsOH \cdot H_2O$ was added to a boiling solution of 110 mg (0.32 mmole) of **11** in 25 ml of absolute toluene and boiled for 20 h. It was then cooled to 20°C, filtered after 3 h, and the sediment was washed with benzene (30 ml). The combined filtrate was evaporated dry in a vacuum at 20°C. The residue was washed with H_2O to pH 7, dried in a vacuum, and sublimated at 120-130°C (10-15 mm Hg), yielding 55 mg (72.3%) of **8**; it was identified with the mp and PMR spectrum.

α,γ-Di-*tert*-butyl-γ-crotonolactone (12). Here 0.3 g of **8** was heated in the open flame of a burner (atm.); the sublimate and still were washed with hexane, filtered, the filtrate was evaporated dry in a vacuum, and the residue was recrystallized from hexane, yielding 37 mg (15.1%) of **12**, white crystals with mp 78-80°C. Found, %: C 73.20; H 10.48. $C_{12}H_{20}O_2$. Calculated, %: C 7343; H 10.27. IR spectrum (ν, cm^{-1}): 1754 (C=O). PMR spectrum ($CDCl_3$): 0.96 s (Me_3C-γ, 9H), 1.26 s (Me_3C-α, 9H), 4.49 d (H_B, 1H, J = 1.6), 6.92 d (H_A, 1H).

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