New synthetic approach to epoxyisoindolo[2,1-*a*]quinolines based on cycloaddition reactions of 2-furyl-substituted tetrahydroquinolines with maleic anhydride and acryloyl chloride

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A procedure was developed for the synthesis of hydrogenated furyl-substituted furo[3,2-*c*]quinolines, pyrano[3,2-*c*]quinolines, and 4-ethoxy- and 4-(2-oxopyrrolidin-1-yl)quinolines. The reactions of these compounds with acryloyl chloride and maleic anhydride produce epoxyisoindolo[2,1-*a*]quinoline derivatives through successive acylation at the quinoline nitrogen atom and intramolecular *exo*-[4+2]-cycloaddition at the furan moiety.

Key words: tetrahydroquinolines, furfurylamines, Povarov reaction, intramolecular Diels—Alder reaction, isoindolo[2,1-*a*]quinolines.

We have synthesized[1] the previously unknown epoxyoxoisoindolo[2,1-*a*]tetrahydroquinolines **1** containing electron-donating substituents R by intramolecular cyclization of 3-metallyl-substituted *N*-aryl-3a,6-epoxytetrahydroisoindol-1-ones under the action of phosphoric acid in 37—67% yields (Scheme 1).

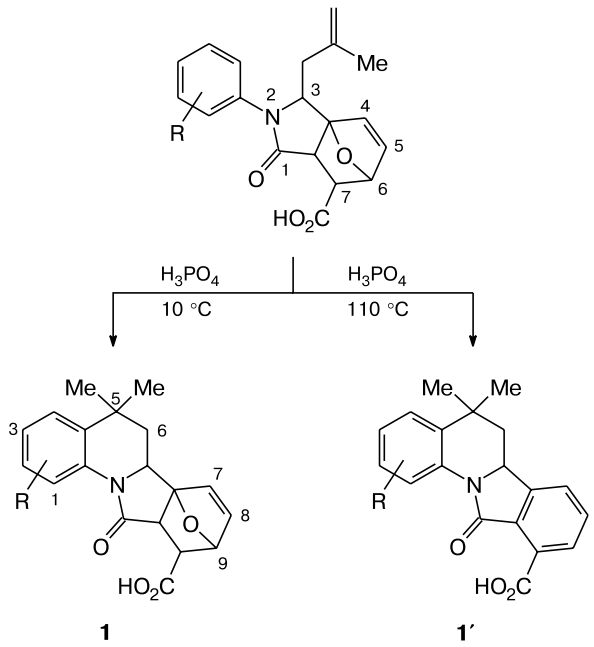
Intramolecular cyclization of epoxyisoindolones containing electron-withdrawing substituents R (see Scheme 1) in the *N*-aryl fragment requires higher temperatures and, as a result, is accompanied by aromatization to give isoindoloquinolines **1´**.[1]

Epoxy compounds **1** are promising synthons for the synthesis of derivatives containing the isoindolo[2,1-*a*]tetrahydroquinoline moiety. Methods for the synthesis of the latter compounds are scarce and involve many steps.[2] It was found that isoindolo[2,1-*a*]tetrahydroquinolines have antihypoxic properties and inhibit human topoisomerase.[3,4]

In the present study, we developed a new synthetic approach to compounds **1** based on the [4+2]-cycloaddition reaction of 4-substituted or 3,4-fused 2-furyltetrahydroquinolines with activated alkenes.

2-Furyl-substituted tetrahydroquinolines required for this investigation were synthesized from furfurylideneanilines **2** and alkenes containing the *N*- or *O*-vinyl fragment by the Povarov reaction in the presence of Lewis acids (LA).[5—8] This reaction was widely used for the synthesis of substituted tetrahydroquinolines,[9—13] including 2-furyl derivatives[7,11,12] (18—41% yields). To optimize this process involving 2-furyl-substituted tetrahydroquinolines **3—5**, we studied the influence of the nature of the catalyst and the solvent and the electronic effects of the substituents in the aryl moiety of furfurylideneanilines **2**.

Scheme 1



1 **1´**

1: R = 3-Me, 3-Pr^i, 1-Et; **1´:** R = 1-Cl, 3-Cl, 3-F

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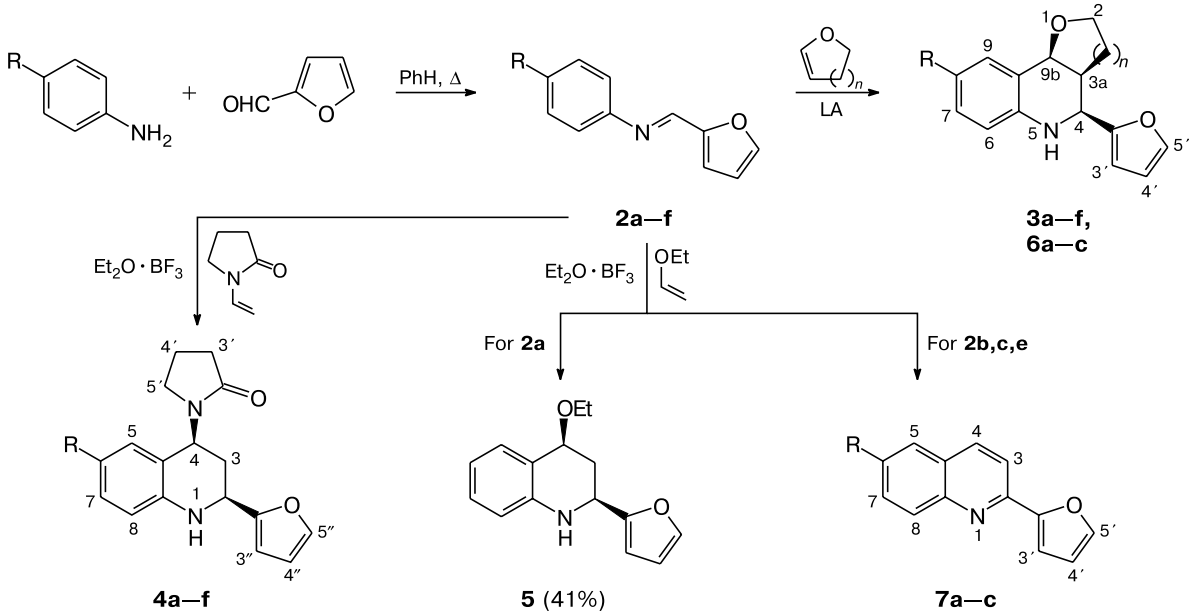
Scheme 2



2—4	R	Yield (%)		Compound	R	Yield (%)
		3	**4**			
a	H	58	80	**6a**	H	7
b	Me	68	43	**6b**	Me	8
c	OMe	64	55	**6c**	F	3
d	Cl	30	67	**7a**	Me	8
e	F	28	72	**7b**	OMe	14
f	NO_2	6	25	**7c**	F	8

n = 1 (**3a—f**), 2 (**6a—c**)

Aldimines **2a—f** were prepared by acid-catalyzed condensation of *para*-substituted anilines with furfural by analogy with the published data[1,14] (Scheme 2).

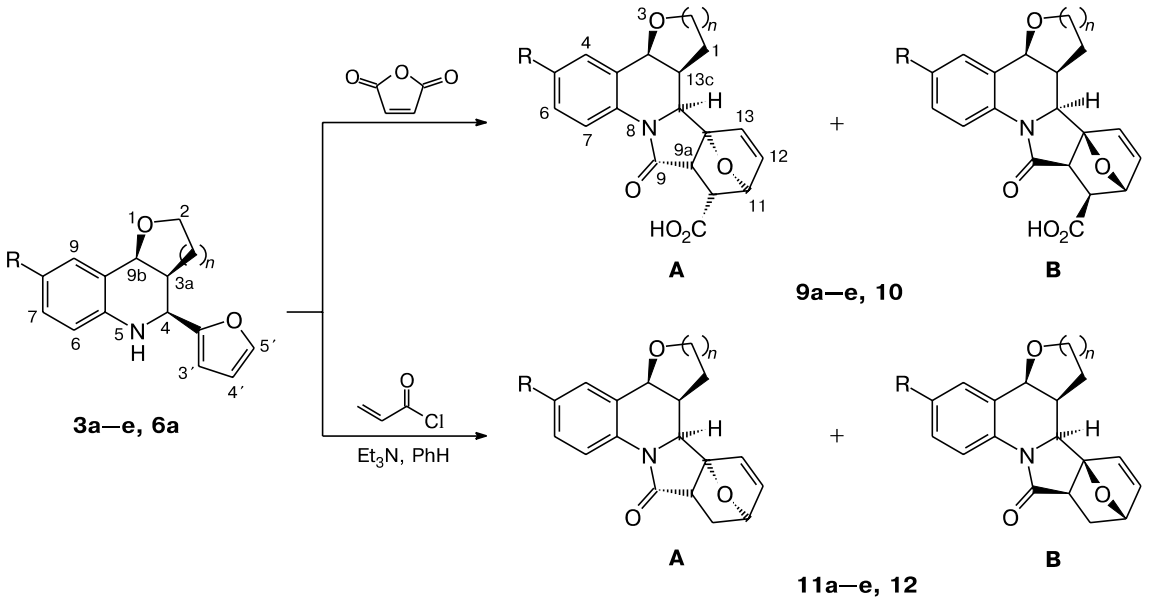
The cycloaddition reactions of aldimines **2a—f** with dihydrofuran, dihydropyran, ethyl vinyl ether, and *N*-vinylpyrrolidin-2-one in the presence of Lewis acids ($ZnCl_2$, ZnI_2, $SnCl_4$, $TiCl_4$, $AlCl_3$, or $Et_2O \cdot BF_3$) or protic acids (trifluoroacetic, oxalic, or *p*-toluenesulfonic acid) were studied. The optimal conditions were found using the reaction of azomethine **2a** with dihydrofuran (see Scheme 2) as a model process.

Strong Lewis acids, *viz.*, $Et_2O \cdot BF_3$ and $AlCl_3$, in anhydrous diethyl ether or benzene proved to be the most efficient catalysts. Under these conditions, the yield of furoquinoline **3a** was 49—58%. Anhydrous oxalic acid and *p*-TsOH in acetonitrile also catalyze cycloaddition (the yield of **3a** was 35—45%). In the presence of other catalysts, the yield of the target product was at most 25%.

The cycloaddition reactions of *N*-vinylpyrrolidone and ethyl vinyl ether with azomethine **2a** proceed analogously. The yields of tetrahydroquinolines **4a** and **5** in the presence of $Et_2O \cdot BF_3$ in anhydrous diethyl ether were 80 and 41%, respectively. Under these conditions, fused tetrahydroquinoline **6a** was synthesized from 3,4-dihydro-2*H*-pyran and Schiff base **2a** in low yield (7%).

The yields of tetrahydroquinolines **3** and **4** substantially depend on the nature of substituents R in the benzene fragment of azomethines **2a—f** (see Scheme 2). Earlier, it has been demonstrated (for the only example[15]) that the electron-withdrawing halogen atoms and the nitro group substantially decrease the yield of furyl-substituted tetrahydroquinolines. This suggests that the Povarov reaction includes the electrophilic attack of the carbocation, which is generated as a result of the addition of alkene to azomethine, on the *N*-aryl fragment. Upon fractionation, 4-ethoxytetrahydroquinolines **5**, which are produced by condensation of azomethines **2b,c,e** with ethyl vinyl ether, eliminate ethanol to give furylquinolines **7a—c** in 8—14% yields. We succeeded in isolating 4-ethoxy-2-furyltetrahydroquinoline (in 41% yield) only with the use of compound **5** having the lowest boiling point. Analogously to 4-alkoxy-2-aryltetrahydroquinolines,[8] 2-furyl-substituted tetrahydroquinoline **5** eliminates an ethanol molecule under the action of HCl in anhydrous diethyl

Scheme 3



3, 9, 11: R = H (**a**), Me (**b**), OMe (**c**), Cl (**d**), F (**e**); *n* = 1
6a, 10, 12: R = H, *n* = 2

ether to give a mixture of unstable 2-furyl-1,2-dihydroquinoline **8** and 2-furylquinoline **7d**.

The structures of compounds **3—6** were confirmed by ^{1}H NMR spectroscopy. For example, the *cis*-dipseudoequatorial arrangement of the substituents at the C(2) and C(4) atoms in compounds **4a—f** and **5** was evidenced by the fact that their ^{1}H NMR spectra show doublets of doublets for the H(2) and H(4) protons with the characteristic spin-spin coupling constants ($J_{H(2),H(3)}$ = 9.1—11.4 Hz, $J_{H(2),H(3)}$ = 2.5—4.9 Hz and $J_{H(4),H(3)}$ = 9.1—12.0 Hz, $J_{H(4),H(3)}$ = 4.9—7.2 Hz, respectively). The spin-spin coupling constants $J_{H(4),H(3a)}$ and $J_{H(3a),H(9b)}$ in the spectra of hexahydrofuroquinolines[9,11,13] **3a—f** and the spin-spin coupling constants $J_{H(4a),H(5)}$ and $J_{H(4a),H(10b)}$ in the spectra of hexahydropyranoquinolines[9,13] **6a—c** confirm the *cis*-arrangement of the substituents at these carbon atoms.

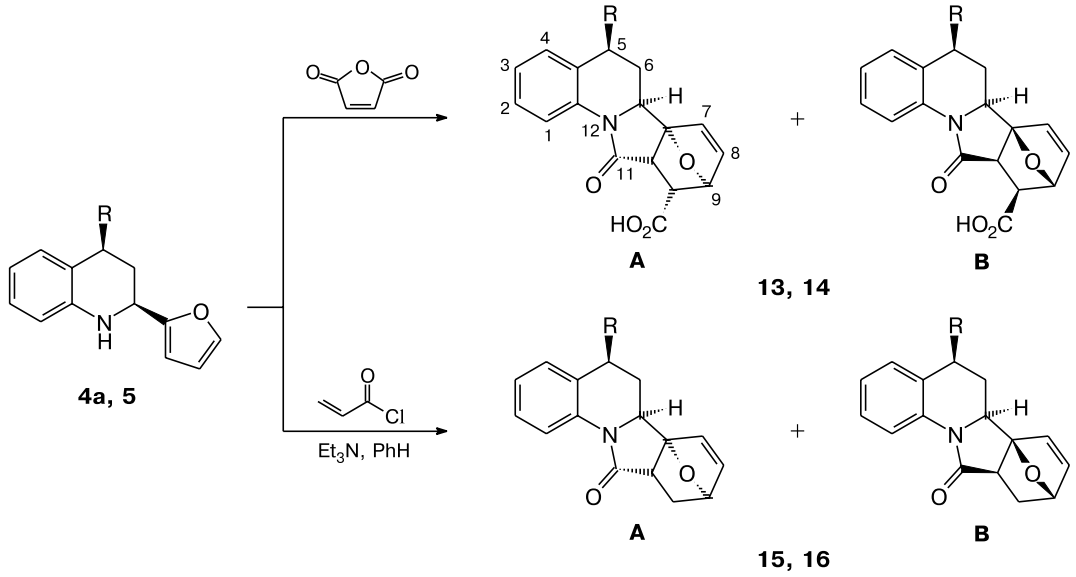
Tetrahydroquinolines **3a—e**, **4a**, **5**, and **6a** are readily involved in the reaction with maleic anhydride (Schemes 3 and 4) to form mixtures of isomeric tetrahydrofuro- (**9**), tetrahydropyrano- (**10**), 4-ethoxy- (**13**), and 4-(2-oxopyrrolidin-1-yl)epoxyisoindolo[2,1-*a*]quinolinecarboxylic acids (**14**) at 0—5 °C. The reactions proceed through initial acylation of the quinoline nitrogen atom followed by intramolecular *exo*-[4+2]-cycloaddition of the unsaturated fragment to the furan moiety.[16,17] Isomers **A** of compounds **9** and **10** with the *trans* arrangement of the epoxide bridge with respect to the substituents in the quinoline ring are generated as the major products in the reactions of 3,4-annelated quinolines **3a—e** and **6a** (see Scheme 3). The cycloaddition reactions of maleic anhydride with 4-substituted tetrahydroquinolines **4a** and **5** (see Scheme 4) produce mainly diastereomers **B** of compounds **13** and **14**, respectively, with the *cis* arrangement of the epoxide oxygen atom with respect to the substituent R (Table 1).

The cycloaddition of maleic anhydride to 3,4-annelated quinolines **3a—e** and **6a** at 140 °C is stereospecific and gives only *trans* isomers **A** of compounds **9** and **10**, repsectively, in 58—100% yields. Under analogous conditions, only *cis* adducts **13B** and **14B** are generated from 4-substituted quinolines **4** and **5**, respectively. According to the ^{1}H NMR spectroscopic data, *cis* isomer **B** is transformed into more stable *trans* isomer **A** by refluxing mix-

Table 1. Ratios of diastereoisomers and the total yields (%, given in parentheses) for the cycloaddition adducts of tetrahydroquinolines **3a—e**, **4a**, **5**, or **6a** and maleic anhydride or acryloyl chloride at different temperatures

Adduct	0—5 °C (*trans*-**A**/*cis*-**B**)	140 °C (isomer)	Adduct	80 °C (*trans*-**A**/*cis*-**B**)
9a	71/29 (65)	*trans*-**A** (85)	**11a**	45/55 (90)
9b	60/40 (74)	*trans*-**A** (94)	**11b**	44/56 (73)
9c	50/50 (99)	*trans*-**A** (100)	**11c**	42/58 (76)
9d	58/42 (65)	*trans*-**A** (70)	**11d**	38/62 (80)
9e	62/38 (70)	*trans*-**A** (80)	**11e**	44/56 (76)
10	95/5 (64)	*trans*-**A** (58)	**12**	33/66 (80)
13	25/75 (88)	*cis*-**B** (99)	**15**	0/100 (53)
14	25/75 (58)	*cis*-**B** (80)	**16**	0/100 (93)

Scheme 4



R = OEt (**5**, **13**, **15**), 2-oxopyrrolidin-1-yl (**4a**, **14**, **16**)

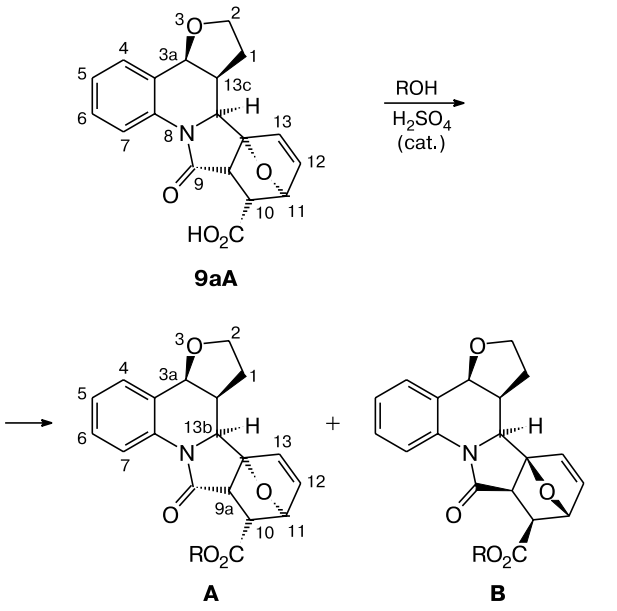
tures of isomers **A** and **B** of compounds **9** and **10** in xylene. This is evidence that the Diels—Alder reaction is reversible. On the contrary, only *cis* isomers **B** are produced by refluxing mixtures of isomers **A** and **B** of compounds **13** and **14**.

Acylation of tetrahydroquinolines **3a—e** and **6a** with acryloyl chloride (see Scheme 3) in boiling benzene in the presence of triethylamine is accompanied by the intramolecular cycloaddition and also affords a mixture of geometric isomers **A** and **B** of epoxyisoindolo[2,1-*a*]quinolines **11** and **12** (see Table 1). The stereoselectivity of cycloaddition is low, the isomer compositions of the mixtures remaining unchanged upon refluxing in xylene. The addition of acryloyl chloride to 4-substituted tetrahydroquinolines **4a** and **5** (see Scheme 4) proceeds stereoselectively; individual *exo-cis* adducts **15B** and **16B** were isolated from the reaction mixture.

Esterification of *trans*-epoxyisoindolo[2,1-*a*]quinolinecarboxylic acid **9aA** with methanol, ethanol, or isopropyl alcohol affords mixtures of esters of *trans*-**A** and *cis*-**B** acids **17—19** (Scheme 5). Taking into account thermodynamic stability of the starting acid **9aA**, it can be hypothesized that its esters **17A—19A** undergo retrodiene decomposition under the reaction conditions. The subsequent intramolecular [4+2]-cycloaddition involving *N*-maleinamide fragments gives rise to mixtures of isomeric esters **17B—19B**. Esterification products **17** and **18** were isolated in the individual form by fractional crystallization (methyl esters **17**) or column chromatography (ethyl esters **18**).

The NMR spectroscopic data did not allow us to unambiguously determine the orientation of the epoxide

Scheme 5



Compound	R	Yield (%)	**A** : **B**
17	Me	80	7 : 1
18	Et	86	1.3 : 1
19	Pr^i	76	1.7 : 1

bridge with respect to the substituents in the quinoline moiety both in the starting isoindoloquinolines **9—16** and esterification products **17—19**. Because of this, we prepared single crystals of methyl esters **17A** and **17B** and

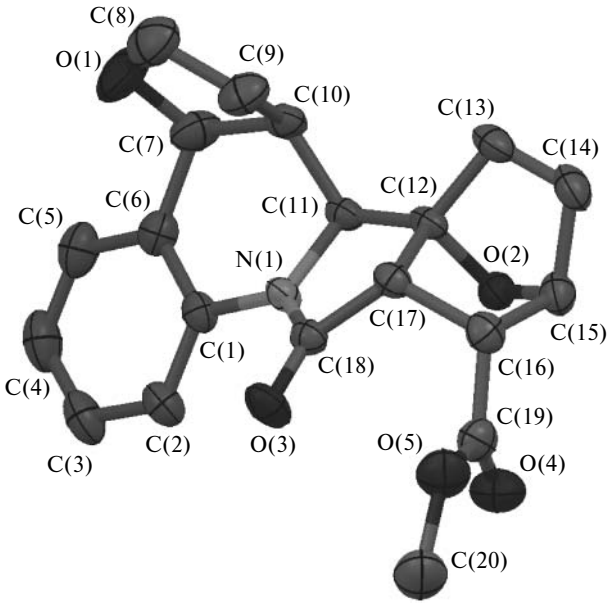


Fig. 1. Molecular structure of major isomer **A** of ester **17**.

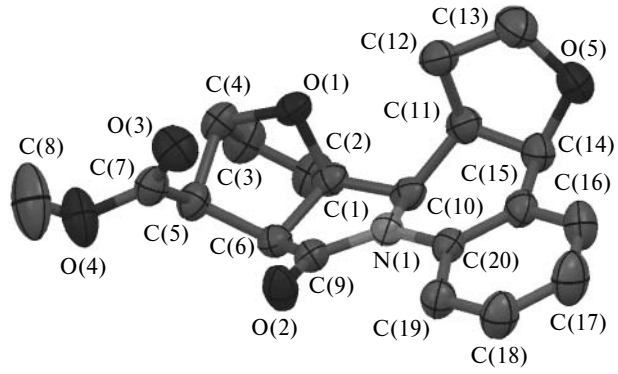


Fig. 2. Molecular structure of minor isomer **B** of ester **17**.

established their molecular structures by X-ray diffraction (Figs 1 and 2).

The tetrahydropyridine moiety in isomer **17A** (see Fig. 1) adopts a sofa conformation with the C(11) atom deviating from the C(1)C(6)C(7)C(10)N(1) plane by 1.258 Å (hereinafter, we use the crystallographic numbering scheme).

In isomer **17B**, this fragment adopts an unsymmetrical chair conformation (see Fig. 2). The deviations of the C(11) and C(10) atoms from the C(14)C(15)C(20)N(1) plane are 0.31 and –0.40 Å, respectively. The tetrahydrofuran ring is *cis*(*a*,*e*)-annelated with the tetrahydroquinoline moiety. The C(7)—O(1) (isomer **17A**) and C(14)—O(5) (isomer **17B**) bonds are pseudoequatorial. In isomer **17A**, the tetrahydrofuran ring is in the *trans* orientation with respect to the epoxide bridge of the oxabicycloheptene fragment; in isomer **17B**, this ring is in the *cis* orientation. In both isomers, the pyrrolidone fragment adopts an envelope conformation with the C(11) (**17A**) and C(1) (**17B**) atoms deviating from the plane through the other four atoms by 0.30 and 0.44 Å, respectively. The configurations of the chiral centers in compounds **17A** and **17B** are completely described in the Experimental section.

Based on the X-ray diffraction data for isomers of **17**, we determined the reference parameters for the ^{1}H and ^{13}C NMR spectra, which allowed the assignment of isomeric epoxyquinolines **9—16** to the *cis* (**B**) or *trans* series (**A**). In particular, the largest difference between the chemical shifts is observed for the protons at the C(7) atom. In the spectra of *trans* isomers **A**, the signal for this proton is shifted upfield compared to that in the spectra of *cis* isomers **B** by $\Delta\delta$ = 0.6—0.8 ppm. For example, the signals for the aromatic H(7) protons in furoisoindoloquinolines **11a—e** are observed at δ 7.91—8.04 (**A**) and 8.57—8.67 (**B**).

This is associated with the difference in the anisotropic deshielding effect of the amide carbonyl group on the *ortho* proton of the benzene ring. According to the X-ray diffraction data for *cis* diastereomer **17B**, the angle between the planes passing through the aromatic ring and the amide group (O(2)C(9)N(1)) is 21°. The corresponding angle in major *trans* isomer **17A** is larger than 35°. Therefore, the *ortho* proton in the latter isomer is virtually outside the deshielding cone of the carbonyl group.

In the ^{13}C NMR spectra, the largest difference between the chemical shifts ($\Delta\delta$ ~3 ppm) is observed for the C(7) and C(13b) atoms. For example, the signals for these atoms in major isomer **17A** are observed at δ 121.2 and 58.8, respectively. In the spectrum of minor isomer **17B**, the corresponding signals are observed at δ 117.9 and 56.2.

To summarize, in the present study we developed an efficient three-step method for the synthesis of epoxyisoindolo[2,1-*a*]quinolines from available starting compounds. The isomer compositions were studied and the three-dimensional structures of the [4+2]-cycloaddition adducts of acryloyl chloride and maleic anhydride with 4-substituted and [*c*]-annelated 1,2,3,4-tetrahydro-2-(2-furyl)quinolines were determined.

Experimental

Reagents were purchased from the Acros Organics and were used without additional purification. The IR spectra were recorded on an Infralum FT-801 Fourier-transform spectrometer in KBr pellets. The ^{1}H NMR spectra were measured on a Bruker WH-400 spectrometer (400.13 MHz) in $CDCl_3$ or DMSO-d_6 at 30 °C using the residual signals of the protons of the solvents (δ 7.26 and 2.49, respectively) as the internal standard. The ^{13}C NMR spectra were recorded on a Bruker Avance 600 spectrometer (150 MHz) using the central signal of the mutiplet of DMSO-d_6 (δ 39.96) as the standard. The assignments of the signals in the spectra were made based on correlation HMQC and COSY-45 experiments. The mass spectra (EI, 70 eV) were

obtained on an HP MS 5988 mass spectrometer or a Finnigan MAT-95-XL GLC-mass spectrometer using a direct inlet system. The TLC analysis was performed on Sorbfil plates (visualization with iodine vapor). Column chromatography was carried out with the use of neutral aluminum oxide (Brockmann activity 0) or Al_2O_3 Fluka-507C (grain size 0.05—0.15 mm).

The melting points, the chromatographic mobilities, parameters of IR and mass spectra, and elemental analysis data for all compounds are given in Table 2. The ratios of isomers in the reaction products were determined from the ^{1}H NMR spectra as the integrated intensity ratios of the analogous protons.

(3a*S,4*S**,9b*S**)-4-(2´-Furyl)-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline (3a), (3a*S**,4*S**,9b*S**)-4-(2´-furyl)-8-methyl-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline (3b), (3a*S**,4*S**,9b*S**)-4-(2´-furyl)-8-methoxy-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline (3c), (3a*S**,4*S**,9b*S**)-8-chloro-4-(2´-furyl)-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline (3d), (3a*S**,4*S**,9b*S**)-8-fluoro-4-(2´-furyl)-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline (3e), and (3a*S**,4*S**,9b*S**)-4-(2´-furyl)-8-nitro-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline (3f) (general procedure).** Aluminum chloride (0.67 g, 5 mmol) (for **2a,d**) or $BF_3 \cdot OEt_2$ (0.63 mL, 5 mmol) (for **2b,c,e,f**) were added

Table 2. Physicochemical characteristics, elemental analysis data, and selected spectroscopic characteristics for tetrahydroquinolines **3a—f**, **4a—f**, **5**, and **6a—c**, quinolines **7a—d**, and isoindolo[2,1-*a*]quinolines **9—19**

Compound	M.p./°C (solvent)	R_f*	Found / Calculated (%)			Molecular formula	MS, m/z ($[M]^+$)	IR, ν/cm^{-1}
			C	H	N			
3a	89—90 (hexane—AcOEt)	0.66	74.55 / 74.67	6.16 / 6.27	5.97 / 5.81	$C_{15}H_{15}NO_2$	241	3345 (NH)
3b	111—112 (hexane—AcOEt)	0.63	75.20 / 75.27	6.61 / 6.71	5.37 / 5.49	$C_{16}H_{17}NO_2$	255	3301 (NH)
3c	119 (hexane—AcOEt)	0.62	70.85 / 70.83	6.25 / 6.32	5.18 / 5.16	$C_{16}H_{17}NO_3$	271	3304 (NH)
3d	105 (hexane—AcOEt)	0.73	65.42 / 65.34	5.13 / 5.12	5.07 / 5.08	$C_{15}H_{14}ClNO_2$	275 (^{35}Cl)	3297 (NH)
3e	101—102 (hexane—AcOEt)	0.58	69.70 / 69.49	5.55 / 5.44	5.49 / 5.40	$C_{15}H_{14}FNO_2$	259	3302 (NH)
3f	217 (Pr^iOH—DMF)	0.50	62.91 / 62.93	4.81 / 4.93	9.77 / 9.79	$C_{15}H_{14}N_2O_4$	286	3267 (NH)
4a	123 (hexane—AcOEt)	0.59	72.49 / 72.32	6.38 / 6.43	9.75 / 9.92	$C_{17}H_{18}N_2O_2$	282	3320 (NH), 1670 (NCO)
4b	188—189 (hexane—AcOEt)	0.70	73.06 / 72.95	6.72 / 6.80	9.51 / 9.45	$C_{18}H_{20}N_2O_2$	296	3315 (NH), 1665 (NCO)
4c	165—166 (hexane—AcOEt)	0.43	69.12 / 69.21	6.53 / 6.45	8.85 / 8.97	$C_{18}H_{20}N_2O_3$	312	3350 (NH), 1680 (NCO)
4d	189 (hexane—AcOEt)	0.49	64.44 / 64.46	5.50 / 5.41	8.82 / 8.84	$C_{17}H_{17}ClN_2O_2$	316 (^{35}Cl)	3326 (NH), 1670 (NCO)
4e	161 (hexane—AcOEt)	0.54	67.87 / 67.99	5.61 / 5.71	9.42 / 9.33	$C_{17}H_{17}FN_2O_2$	300	3364 (NH), 1670 (NCO)
4f	212 (Pr^iOH—DMF)	0.43	62.33 / 62.38	5.30 / 5.23	12.75 / 12.84	$C_{17}H_{17}N_3O_4$	327	3295 (NH), 1669 (NCO)
5	60—61 (hexane—AcOEt)	0.61	73.23 / 74.05	6.96 / 7.04	5.86 / 5.76	$C_{15}H_{17}NO_2$	243	3380 (NH)
6a	152—153 (hexane—AcOEt)	0.63	75.17 / 75.27	6.50 / 6.71	5.50 / 5.49	$C_{16}H_{17}NO_2$	255	3310 (NH)
6b	118 (hexane—AcOEt)	0.72	75.85 / 75.81	7.12 / 7.11	5.23 / 5.20	$C_{17}H_{19}NO_2$	269	3312 (NH)
6c	119 (hexane—AcOEt)	0.70	70.25 / 70.31	5.95 / 5.90	5.02 / 5.12	$C_{16}H_{16}FNO_2$	273	3325 (NH)
7a	73—74 (hexane—AcOEt)	0.72	80.37 / 80.36	5.24 / 5.30	6.61 / 6.69	$C_{14}H_{11}NO$	209	1623 (C=C)
7b	80—82 (hexane—AcOEt)	0.37	74.68 / 74.65	4.80 / 4.92	6.27 / 6.22	$C_{14}H_{11}NO_2$	225	1621 (C=C)
7c	76—78 (hexane—AcOEt)	0.68	73.14 / 73.23	3.65 / 3.78	6.51 / 6.57	$C_{13}H_8FNO$	213	1622 (C=C)

(*to be continued*)

Table 2 (*continued*)

Compound	M.p./°C (solvent)	R_f*	Found / Calculated (%)			Molecular formula	MS, m/z ($[M]^+$)	IR, ν/cm^{-1}
			C	H	N			
7d	58—59	0.62	80.01	4.65	7.16	$C_{13}H_9NO$	195	1615 (C=C)
	(hexane—AcOEt)		79.98	4.65	7.17			
9aA	192—193	—	67.25	5.03	4.21	$C_{19}H_{17}NO_5$	339	1700 (NCO),
	(Pr^iOH—DMF)		67.25	5.05	4.13			1725 (CO_2H)
9bA	208—210	—	68.11	5.51	3.93	$C_{20}H_{19}NO_5$	353	1701 (NCO),
	(Pr^iOH—DMF)		67.98	5.42	3.96			1726 (CO_2H)
9cA	204—206	—	65.03	5.27	3.77	$C_{20}H_{19}NO_6$	369	1687 (NCO),
	(Pr^iOH—DMF)		65.03	5.18	3.79			1727 (CO_2H)
9dA	178—180	—	61.15	4.35	3.68	$C_{19}H_{16}ClNO_5$	373 (^{35}Cl)	1701 (NCO),
	(Pr^iOH—DMF)		61.05	4.31	3.75			1724 (CO_2H)
9eA	205—207	—	63.82	4.58	3.80	$C_{19}H_{16}FNO_5$	357	1674 (NCO),
	(Pr^iOH—DMF)		63.86	4.51	3.92			1735 (CO_2H)
10A	221—222	—	70.16	5.49	3.78	$C_{20}H_{19}NO_5$	353	1655 (NCO),
	(Pr^iOH—DMF)		67.98	5.42	3.96			1710 (CO_2H)
11a	92—95	0.52,	73.13	5.81	4.79	$C_{18}H_{17}NO_3$	295	1685 (NCO)
(**A** + **B**)	(hexane—AcOEt)	0.20	73.20	5.80	4.74			
11b	84—86	0.54,	73.73	6.11	4.41	$C_{19}H_{19}NO_3$	309	1688 (NCO)
(**A** + **B**)	(hexane—AcOEt)	0.34	73.77	6.19	4.53			
11c	84—86	0.44,	70.23	5.84	4.22	$C_{19}H_{19}NO_4$	325	1685 (NCO)
(**A** + **B**)	(hexane—AcOEt)	0.22	70.14	5.89	4.31			
11d	126—128	0.33,	65.64	4.87	4.25	$C_{18}H_{16}ClNO_3$	329 (^{35}Cl)	1690 (NCO)
(**A** + **B**)	(hexane—AcOEt)	0.30	65.56	4.89	4.25			
11e	118	0.36,	68.89	5.05	4.42	$C_{18}H_{16}FNO_3$	313	1692 (NCO)
(**A** + **B**)	(hexane—AcOEt)	0.34	69.00	5.15	4.47			
12	154—160	0.33,	73.52	6.13	4.42	$C_{19}H_{19}NO_3$	309	1690 (NCO)
(**A** + **B**)	(hexane—AcOEt)	0.46	73.77	6.19	4.53			
13B	200—201	—	66.84	5.62	4.31	$C_{19}H_{19}NO_5$	341	1700 (NCO),
	(Pr^iOH—DMF)		66.85	5.61	4.10			1730 (CO_2H)
14B	253—254	—	66.21	5.42	7.52	$C_{21}H_{20}N_2O_5$	380	1691, 1638 (NCO),
	(Pr^iOH—DMF)		66.31	5.30	7.36			1733 (CO_2H)
15B	128	0.33	72.84	6.48	4.67	$C_{18}H_{19}NO_3$	297	1685 (NCO)
	(hexane—AcOEt)		72.71	6.44	4.71			
16B	210	0.59	71.55	6.08	8.69	$C_{20}H_{20}N_2O_3$	336	1695 (NCO),
	(hexane—AcOEt)		71.41	5.99	8.33			1673 (NCO)
17	201—202	0.44	67.79	5.32	3.99	$C_{20}H_{19}NO_5$	353	1688 (NCO),
(**A** + **B**)	(hexane—AcOEt)		67.98	5.42	3.96			1731 (CO_2Me)
18	166—168	0.53	68.78	5.79	3.71	$C_{21}H_{21}NO_5$	367	1688 (NCO),
(**A** + **B**)	(hexane—AcOEt)		68.65	5.76	3.81			1720 (CO_2Et)
19	158	0.52	69.12	5.93	3.35	$C_{22}H_{23}NO_5$	381	1689 (NCO),
(**A** + **B**)	(hexane—AcOEt)		69.28	6.08	3.67			1728 (CO_2Pr^i)

* An AcOEt—hexane mixture as the eluent: 1 : 4 (for **3a,c**); 1 : 8 (for **3b**, **6a—c**, and **7a,b**); 1 : 6 (for **3d,e** and **7d**); 2 : 1 (for **3f** and **4a,b,f**); 3 : 1 (for **4c**); 1 : 1 (for **4d,e**, **11a—e**, **12**, **15**, and **17—19**); 1 : 10 (for **5** and **7c**); and 1 : 2 (for **11d,e** (the first value)). An AcOEt—EtOH, 3 : 1, mixture as the eluent (for **16**).

to a stirred solution of azomethine **2** (0.2 mol) in benzene (100 mL) (for **2a—e**) or dichloromethane (100 mL) (for **2f**) at 0 °C. Then dihydrofuran (16.6 mL, 0.22 mol) was added dropwise. The reaction mixture was stirred at 0—5 °C for 2 h and at 20 °C for 3 h. Then a 25% aqueous ammonia solution (3—4 mL) was added until pH became alkaline and concentrated under vacuum. The residue (viscous dark oil) was purified by column chromatography using a 1 : 10 AcOEt—hexane mixture as the eluent. Tetrahydrofuroquinolines **3a—f** were obtained as white crystals. The spectroscopic characteristics of these compounds are given in Tables 3 and 4.

(2*S,4*S**)-2-(2′-Furyl)-4-(2-oxopyrrolidin-1-yl)-1,2,3,4-tetrahydroquinoline (4a), (2*S**,4*S**)-2-(2′-furyl)-6-methyl-4-(2-oxopyrrolidin-1-yl)-1,2,3,4-tetrahydroquinoline (4b), (2*S**,4*S**)-2-(2′-furyl)-6-methoxy-4-(2-oxopyrrolidin-1-yl)-1,2,3,4-tetrahydroquinoline (4c), (2*S**,4*S**)-6-chloro-2-(2′-furyl)-4-(2-oxopyrrolidin-1-yl)-1,2,3,4-tetrahydroquinoline (4d), (2*S**,4*S**)-6-fluoro-2-(2′-furyl)-4-(2-oxopyrrolidin-1-yl)-**

Table 3. Chemical shifts (δ) of protons in the ^{1}H NMR spectra of compounds **3a—f** in $CDCl_3$

Compound	δ															
	H(2A)	H(2B)	H(3a) (dq)	H(3A) (ddt)	H(3B) (dddd)	H(4) (d)	H(6)	H(7)	H(8)	H(9)	H(9b) (d)	H(5′) (dd)	H(4′)	H(3′)	NH (br.s)	Other protons
3a	3.78 (q)	3.75 (dt)	2.95	2.19	1.82	4.69	7.33 (dd)	6.81 (dt)	7.07 (dt)	6.58 (dd)	5.22	7.38	6.36 (dd)	6.26 (dd)	3.95	—
3b	3.80—3.76 (m)		2.97	2.22	1.83	4.66	6.54 (d)	7.98 (dd)	—	7.17 (br.s)	5.21	7.40	6.38 (dd)	6.29 (dt)	3.84	2.27 (s, Me)
3c	3.82—3.73 (m)		2.95	2.20	1.82	4.63	6.56 (d)	6.71 (dd)	—	6.90 (d)	5.20	7.38	6.36 (br.d)	6.27 (dd)	3.75	3.75 (s, OMe)
3d	3.80 (q)	3.75 (dt)	2.94	2.16	1.85	4.69	6.53 (d)	7.02 (dd)	—	7.31 (br.d)	5.16	7.39	6.37 (dd)	6.28 (dd)	3.97	—
3e	3.80 (q)	3.75 (dt)	2.95	2.18	1.84	4.67	6.55 (dd)	6.81 (dd)	—	7.05 (dd)	5.18	7.40	6.37 (dd)	6.28 (dd)	3.89	—
3f	3.86 (q)	3.76 (dt)	2.96	2.09	1.93	4.89	6.56 (d)	7.98 (dd)	—	8.30 (br.d)	5.21	7.42	6.40 (dd)	6.32 (dd)	4.69	—

Table 4. Spin-spin coupling constants (J) of protons in the ^{1}H NMR spectra of compounds **3a—f** in $CDCl_3$

Compound	J/Hz																	
	2A, 2B	2A, 3A	2A, 3B	2B, 3A	2B, 3B	3A, 3B	3A, 3a	3B, 3a	3a, 4	3a, 9b	6, 7	6, 8	7, 8	7, 9	8, 9	5′, 4′	5′, 3′	4′, 3′
3a	7.3	7.3	4.7	8.6	7.3	12.3	8.8	8.8	3.0	7.9	7.7	1.2	7.7	1.2	7.7	1.8	0.8	3.4
3b	—*	8.6	4.9	8.6	6.7	12.0	8.6	8.8	2.9	8.0	8.1	—	—	1.5	—	1.8	0.8	3.2
3c	—*	9.0	4.7	9.0	7.2	12.2	8.5	8.8	3.0	7.9	8.7	—	—	2.8	—	1.7	0.7	3.2
3d	8.2	—*	4.5	8.5	7.4	12.2	—*	8.7	2.9	7.8	8.6	—	—	2.5	—	1.8	0.8	3.2
3e**	8.4	—*	4.5	8.5	7.4	12.6	8.8	8.7	2.5	7.9	8.8	—	—	3.0	—	1.6	0.6	3.2
3f	—*	—*	4.3	8.5	—*	—*	—*	8.8	3.5	7.4	9.0	—	—	2.6	—	1.8	0.7	3.3

* The spin-spin coupling constants were not determined.
** $J_{F,9}$ = 9.0 Hz and $J_{F,6}$ = 4.7 Hz.

1,2,3,4-tetrahydroquinoline (4e), and (2*S,4*S**)-2-(2´-furyl)-6-nitro-4-(2-oxopyrrolidin-1-yl)-1,2,3,4-tetrahydroquinoline (4f) (general procedure).** Boron trifluoride etherate (0.63 mL, 5 mmol) and *N*-vinylpyrrolidin-2-one (23.4 mL, 0.22 mol) were successively added to a stirred solution of azomethine **2** (0.2 mol) in anhydrous diethyl ether (100 mL) (for **4a—e**) or dry dichloromethane (100 mL) (for **4f**) at 25 °C. The reaction mixture was stirred at 20 °C for 1 day (TLC monitoring). Then a 25% aqueous ammonia solution (3—4 mL) was added, and the solvent was removed under reduced pressure. The residue (viscous brown oil) was purified by column chromatography using diethyl ether as the eluent. Tetrahydroquinolines **4a—f** were obtained as white crystals. The spectroscopic characteristics of these compounds are given in Tables 5 and 6.

(2*S,4*S**)-4-Ethoxy-2-(2´-furyl)-1,2,3,4-tetrahydroquinoline (5).** Boron trifluoride etherate (0.4 mL, 3.0 mmol) and ethyl vinyl ether (21.8 mL, 0.23 mol) were added with stirring to a solution of furfurylideneaniline (**2a**) (38.89 g, 0.23 mol) in anhydrous diethyl ether (100 mL) at 25 °C. The reaction mixture was stirred at 20 °C for 3 h (TLC monitoring) and successively washed with a 5% sodium hydroxide solution (50 mL) and water (100 mL). The organic phase was dried with magnesium sulfate. The solvent was removed, and the residue was fractionated under vacuum. Compound **5** was obtained in a yield of 22.65 g (0.09 mol) as a yellow oil (b.p. 167—169 °C (3 Torr)), which rapidly crystallized. Yellow crystals, the yield was 41%. MS, m/z (I_{rel} (%)): 243 $[M]^+$ (37), 196 (80), 167 (48), 130 (100), 77 (55), 39 (82). ^{1}H NMR ($CDCl_3$), δ: 7.39 (dd, 1 H, H(5´), $J_{5',3'}$ = 0.8 Hz, $J_{5',4'}$ = 1.8 Hz); 7.37 (dd, 1 H, H(5), $J_{5,6}$ = 7.4 Hz); 7.06 (ddd, 1 H, H(7), $J_{5,7}$ = 1.6 Hz, $J_{6,7}$ = 7.4 Hz, $J_{7,8}$ = 8.0 Hz); 6.75 (dt, 1 H, H(6), $J_{6,8}$ = 1.0 Hz, $J_{5,6}$ = $J_{6,7}$ = 7.4 Hz); 6.55 (dd, 1 H, H(8), $J_{6,8}$ = 1.0 Hz, $J_{7,8}$ = 8.0 Hz); 6.35 (dd, 1 H, H(4´), $J_{5',4'}$ = 1.8 Hz, $J_{4',3'}$ = 3.2 Hz); 6.26 (dd, 1 H, H(3´), $J_{5',3'}$ = 0.8 Hz, $J_{4',3'}$ = 3.2 Hz); 4.76 (dd, 1 H, H_{ax}(4), $J_{3eq,4ax}$ = 5.6 Hz, $J_{3ax,4ax}$ = 9.9 Hz); 4.63 (dd, 1 H, H_{ax}(2), $J_{2ax,3eq}$ = 2.6 Hz, $J_{2ax,3ax}$ = 10.9 Hz); 4.08 (br.s, 1 H, NH); 3.73—3.58 (m, 2 H, OC$\underline{H}_2$CH$_3$, J = 7.0 Hz); 2.52 (ddd, 1 H, H_{eq}(3), $J_{2ax,3eq}$ = 2.6 Hz, $J_{3,3}$ = 12.4 Hz, $J_{3eq,4ax}$ = 5.6 Hz); 2.22 (ddd, H_{ax}(3), $J_{3ax,4ax}$ = 9.9 Hz, $J_{2ax,3ax}$ = 10.9 Hz, $J_{3,3}$ = 12.4 Hz); 1.27 (t, 3 H, OCH$_2$C$\underline{H}_3$, J = 7.0 Hz).

(4a*S,5*S**,10b*S**)-5-(2´-Furyl)-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline (6a), (4a*S**,5*S**,10b*S**)-5-(2´-furyl)-9-methyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline (6b), and (4a*S**,5*S**,10b*S**)-9-fluoro-5-(2´-furyl)-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline (6c) (general procedure).** Boron trifluoride etherate (0.3 mL, 25 mmol) and dihydropyran (10 mL, 0.11 mol) were successively added to a stirred solution of azomethine **2** (0.1 mol) in dry benzene (100 mL), the temperature of the reaction mixture being raised to 50 °C. The reaction mixture was stirred at 20 °C for 1 day. Then a 25% aqueous ammonia solution (3—4 mL) was added, the solvent was removed, and the residue was fractionated under vacuum (**6a**) or purified by column chromatography (**6b,c**). Pyranoquinolines **6a—c** were obtained as white crystals. The spectroscopic characteristics of these compounds are given in Tables 7 and 8.

2-(2´-Furyl)-6-methylquinoline (7a), 2-(2´-furyl)-6-methoxyquinoline (7b), and 6-fluoro-2-(2´-furyl)quinoline (7c) (general procedure). Boron trifluoride etherate (0.3 mL, 25 mmol) was added to a stirred solution of azomethine **2** (0.1 mol) in anhydrous diethyl ether (100 mL) (for **7a**,**c**) or dichloromethane (100 mL) (for **7b**). Then ethyl vinyl ether (9.6 mL, 0.1 mol) was added dropwise at 0 °C. The reaction mixture was stirred at ~20 °C for 1 day (TLC monitoring), a 25% aqueous ammonia solution (3—4 mL) was added until pH became highly alkaline, the solvent was evaporated, and the residue was fractionated under vacuum (**7a,c**) or purified by column chromatography (**7b**) (AcOEt—hexane, 1 : 10, as the eluent). Furyl-substituted quinolines **7a—c** were obtained as white crystals. The spectroscopic characteristics of these compounds are given in Table 9.

(3a*S,9a*S**,10*R**,11*S**,13a*R**,13b*S**,13c*S**)-9-Oxo-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinoline-10-carboxylic acid (9aA), (3a*S**,9a*R**,10*S**,11*R**,13a*S**,13b*S**,13c*S**)-9-oxo-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinoline-10-carboxylic acid (9aB), (3a*S**,9a*S**,10*R**,11*S**,13a*R**,13b*S**,13c*S**)-5-methyl-9-oxo-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinoline-10-carboxylic acid (9bA), (3a*S**,9a*R**,10*S**,11*R**,13a*S**,13b*S**,13c*S**)-5-methyl-9-oxo-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinoline-10-carboxylic acid (9bB), (3a*S**,9a*S**,10*R**,11*S**,13a*R**,13b*S**,13c*S**)-5-methoxy-9-oxo-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinoline-10-carboxylic acid (9cA), (3a*S**,9a*R**,10*S**,11*R**,13a*S**,13b*S**,13c*S**)-5-methoxy-9-oxo-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinoline-10-carboxylic acid (9cB), (3a*S**,9a*S**,10*R**,11*S**,13a*R**,13b*S**,13c*S**)-5-chloro-9-oxo-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinoline-10-carboxylic acid (9dA), (3a*S**,9a*R**,10*S**,11*R**,13a*S**,13b*S**,13c*S**)-5-chloro-9-oxo-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinoline-10-carboxylic acid (9dB), (3a*S**,9a*S**,10*R**,11*S**,13a*R**,13b*S**,13c*S**)-5-fluoro-9-oxo-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinoline-10-carboxylic acid (9eA), and (3a*S**,9a*R**,10*S**,11*R**,13a*S**,13b*S**,13c*S**)-5-fluoro-9-oxo-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinoline-10-carboxylic acid (9eB) (general procedure *A*).** A solution of maleic anhydride (0.43 g, 4.36 mmol) in toluene (10 mL) was added to a solution of amine **3a—e** (4.15 mmol) in toluene (10 mL) at 0—3 °C. The reaction mixture was kept at 0—3 °C for 3 days (TLC monitoring). The white crystals that formed were filtered off, and mixtures of isomers **A** and **B** of the corresponding carboxylic acids **9a—e** were obtained. The ratios of isomers and spectroscopic characteristics are given in Tables 1, 10, and 11.

General procedure *B*. A solution of tetrahydroquinoline **3a—e** (4.15 mmol) and maleic anhydride (0.43 g, 4.36 mmol) in toluene (20 mL) was refluxed for 2—10 h (TLC monitoring). The white crystals that formed were filtered off, and carboxylic acids **9aA—9eA** were obtained.

(3a*S,9a*S**,11*R**,13a*R**,13b*S**,13c*S**)-1,2,10,11,13b,13c-Hexahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinolin-9(9a*H*)-one (11aA), (3a*S**,9a*R**,11*S**,13a*S**,13b*S**,13c*S**)-1,2,10,11,13b,13c-hexahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinolin-9(9a*H*)-one (11aB), (3a*S**,9a*S**,11*R**,13a*R**,13b*S**,13c*S**)-5-methyl-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinolin-9(9a*H*)-one (11bA), (3a*S**,9a*R**,11*S**,13a*S**,13b*S**,13c*S**)-5-methyl-**

Table 5. Chemical shifts (δ) of protons in the ^{1}H NMR spectra of compounds **4a—f** in $CDCl_3$

Compound	δ															
	$H_{ax}(2)$	$H_{eq}(3)$	$H_{ax}(3)$	H(3′) (m)	$H_{ax}(4)$	H(4′) (m)	H(5′A)	H(5′B)	H(5)	H(6)	H(7)	H(8)	H(5″) (dd)	H(4″)	H(3″)	NH (br.s)	Other protons
4a	4.68 (dd)	2.27—2.17 (m)		2.59—2.49	5.69 (dd)	2.06—1.99	3.29—3.15 (m)		6.87 (d)	6.72 (br.t)	7.05 (dt)	6.59 (d)	7.40	6.36 (dd)	6.26 (dd)	4.10	—
4b	4.61 (dd)	2.25—2.19 (m)		2.94—2.49	5.66 (dd)	2.04—2.00	3.25 (dt)		6.67 (s)	—	6.86 (br.d)	6.52 (d)	7.38	6.35 (dd)	6.25 (dd)	4.01	2.21 (s, Me)
4c	4.63 (dd)	2.29 (ddd)	2.24 (ddd)	2.60—2.45	5.70 (dd)	2.08—2.00	3.31—3.17 (m)		6.49 (d)	—	6.71 (dd)	6.59 (d)	7.41	6.37 (dd)	6.28 (dd)	1.67	3.74 (s, OMe)
4d	4.65 (m)	2.24—2.17 (m)		2.60—2.43	5.63 (br.t)	2.09—2.01	3.29—3.15 (m)		6.81 (dd)	—	6.99 (dd)	6.51 (d)	7.39	6.35 (dd)	6.26 (br.d)	4.14	—
4e	4.65 (dd)	2.00 (ddd)	2.09 (q)	2.40—2.30	5.40 (dd)	2.03—1.89	3.23 (dt)	3.00 (m)	6.49 (dd)	—	6.82 (dt)	6.65 (dd)	7.62	6.44 (dd)	6.37 (dd)	6.04	—
4f	4.96 (dd)	2.06 (ddd)	2.19 (q)	2.42—2.32	5.41 (dd)	2.01—1.93	3.30 (dt)	3.09 (ddd)	7.50 (dd)	—	7.89 (dd)	6.72 (d)	7.68	6.47 (m)	6.47 (m)	7.79	—

Table 6. Spin-spin coupling constants (J) of protons in the ^{1}H NMR spectra of compounds **4a—f** in $CDCl_3$

Compound	J/Hz												
	2, 3_{ax}	2, 3_{eq}	3_{ax}, 3_{eq}	3_{ax}, 4	3_{eq}, 4	5, 6	5, 7	5, 8	6, 7	7, 8	5″, 4″	5″, 3″	4″, 3″
4a	9.7	4.0	—*	10.7	7.2	7.6	—	—	7.6	8.1	1.8	0.8	3.0
4b	10.3	3.1	—*	10.9	6.9	—	—	—	—	8.1	1.8	0.8	3.2
4c	11.1	2.5	12.3	11.6	6.6	—	2.8	—	—	8.7	1.8	0.8	3.2
4d	9.1	4.9	—*	9.1	5.2	—	2.4	0.9	—	8.6	1.7	0.6	3.2
4e**	11.1	2.5	11.5	12.1	6.0	—	2.8	—	—	8.7	1.8	0.7	3.2
4f	11.4	3.2	12.0	12.0	4.9	—	2.6	0.7	—	9.1	1.5	0.9	3.2

* The spin-spin coupling constants were not determined.
** $J_{F,8}$ = 5.0 Hz, $J_{F,7}$ = 8.5 Hz, and $J_{F,5}$ = 9.6 Hz.

Table 7. Chemical shifts (δ) of protons in the ^{1}H NMR spectra of compounds **6a—c** in $CDCl_3$

Compound	δ														
	H(2A)	H(2B) (dt)	H(3), H(4) (m)	H(4a) (m)	H(5) (d)	H(7)	H(8)	H(9)	H(10)	H(10b) (d)	H(5′) (dd)	H(4′)	H(3′) (dd)	NH (br.s)	Other protons
6a	3.60 (br.dd)	3.41	1.67—1.45	2.38	4.71	6.60 (d)	7.10 (dt)	6.81 (br.d)	7.42 (br.d)	5.24	7.41	6.40 (d)	6.30	3.96	—
6b	3.61 (m)	3.43	1.69—1.45	2.37	4.67	6.53 (d)	6.91 (ddq)	—	7.24 (br.d)	5.21	7.39	6.37 (dd)	6.29	3.84	2.28 (s, Me)
6c	3.62 (dd)	3.39	1.69—1.46	2.37	4.67	6.54 (dd)	6.81 (dt)	—	7.14 (dd)	5.19	7.40	6.38 (dd)	6.29	3.87	—

Table 8. Spin-spin coupling constants (J) of protons in the ^{1}H NMR spectra of compounds **6a—c** in $CDCl_3$

Compound	J/Hz												
	2A, 2B	2A, 3	2B, 3	4a, 5	4a, 10b	7, 8	8, 9	8, 10	9, 10	5′, 4′	5′, 3′	4′, 3′	Other coupling constants
6a	11.3	3.4	—*	2.1	5.7	8.0	7.5	1.7	7.5	1.6	0.8	3.2	—
6b	11.6	—*	1.5	2.2	5.6	8.0	—	1.2	—	1.7	0.7	3.2	—
6c	11.4	4.5	2.0	2.0	5.6	8.8	—	2.9	—	1.8	0.9	3.0	$J_{7,F} = 4.6$, $J_{8,F} = 9.5$, $J_{10,F} = 9.5$

* The spin-spin coupling constants were not determined.

Table 9. Chemical shifts (δ) and spin-spin coupling constants (J) of protons in the ^{1}H NMR spectra of compounds **7a—c** in $CDCl_3$

Compound	δ									J/Hz						
	H(3) (d)	H(4) (d)	H(5)	H(7)	H(8)	H(5′)	H(4′) (dd)	H(3′)	Other protons	3, 4	5, 7	7, 8	5′, 4′	5′, 3′	4′, 3′	Other coupling constants
7a	7.78	8.07	7.54 (m)		8.02 (d)	7.62 (dd)	6.58	7.18 (dd)	2.53 (s, Me)	8.7	—	9.3	1.7	0.8	3.4	—
7b	7.83	8.11	7.14 (d)	7.58 (m)	8.11 (dd)	7.63 (dd)	6.59	7.19 (dd)	—	8.6	2.9	8.6	1.8	0.7	3.4	$J_{F,8} = 5.9$, $J_{F,7} = 9.5$, $J_{F,5} = 8.6$
7c	7.77	8.05	7.05 (d)	7.36 (dd)	8.03 (d)	7.60 (br.d)	6.57	7.14 (br.d)	3.50 (s, OMe)	8.6	2.5	9.2	1.8	0.8	3.1	—

Table 10. Chemical shifts (δ) of protons in the ^{1}H NMR spectra of compounds **9a—e** in DMSO-d_6

Compound	δ																
	H(1A)	H(1B)	H(2A)	H(2B)	H(3a) (d)	H(4)	H(5)	H(6)	H(7)	H(9a)	H(10) (d)	H(11)	H(12) (dd)	H(13)	H(13b) (d)	H(13c)	Other protons
9aA	1.57 (tt)	2.10 (dddd)	3.77 (dt)	3.70 (dt)	5.29	7.36 (dd)	7.27 (dt)	7.15 (dt)	7.76 (dd)	2.64	3.06	5.08	6.54	6.86	4.47	3.13 (ddt)	12.40 (br.s, CO_2H)
9aB	1.69 (tt)	1.98 (ddt)	3.71 (dt)	3.46 (dt)	5.20	7.36 (d)	7.23 (dt)	7.08 (dt)	8.56 (d)	2.55	3.11	5.08	6.50	6.61	4.92	2.82 (m)	12.40 (br.s, CO_2H)
9bA	1.55 (tt)	2.09 (m)	3.76 (dt)	3.70 (dt)	5.25	7.16 (dd)	—	7.08 (dd)	7.63 (d)	2.62	3.03	5.07	6.53	6.85	4.42	3.11 (ddt)	2.26 (s, Me)
9bB	1.69 (tt)	1.98 (m)	3.47 (m)		5.17	7.16 (d)	—	7.04 (dd)	8.45 (d)	2.55	3.09	5.08	6.49	6.71	4.89	2.80 (m)	2.52 (s, Me)
9cA	1.53 (tt)	2.08 (m)	3.76 (dt)	3.71 (dt)	5.24	7.15 (dd)	—	7.07 (dd)	7.65 (d)	2.60	3.00	5.06	6.52	6.84	4.40	3.11 (ddt)	3.75 (s, OMe)
9cB	1.67 (tt)	1.97 (tt)	3.72 (dt)	3.47 (dt)	5.16	6.88 (d)	—	6.82 (dd)	8.49 (d)	2.53	3.07	5.06	6.48	6.60	4.86	2.80 (m)	3.71 (s, OMe)
9dA	1.54 (m)	2.10 (m)	3.81—3.70 (m)		5.27	7.36 (dd)	—	7.34 (dd)	7.77 (d)	2.62	3.06	5.08	6.54	6.86	4.50	3.12 (m)	12.80 (br.s, CO_2H)
9dB	1.65 (m)	1.98 (m)	3.51 (m)		5.19	7.34 (dd)	—	7.30 (dd)	8.58 (d)	2.56	3.12	5.08	6.50	6.60	4.93	2.84 (m)	12.80 (br.s, CO_2H)
9eA	1.53 (m)	2.09 (m)	3.74 (m)		5.27	7.15 (m)	—	7.15 (m)	7.76 (d)	2.62	3.04	5.07	6.53	6.86	4.48	3.12 (m)	11.80 (br.s, CO_2H)
9eB	1.65 (m)	1.99 (m)	3.72 (m)		5.19	7.15 (m)	—	7.15 (m)	8.62 (d)	2.58	3.12	5.07	6.50	6.61	4.93	2.84 (m)	11.80 (br.s, CO_2H)

Table 11. Spin-spin coupling constants (J) of protons in the ^{1}H NMR spectra of compounds **9a—e** in DMSO-d_6

Compound	J/Hz																	
	1A, 1B	1A, 2A	1A, 2B	1B, 2A	1B, 2B	1A, 13c	1B, 13c	2A, 2B	3a, 13c	4, 5	4, 6	5, 6	5, 7	6, 7	9a, 10	11, 12	12, 13	13b, 13c
9aA	11.2	6.5	3.0	8.7	8.7	8.1	10.9	8.4	8.2	7.9	1.1	7.9	1.1	7.9	9.2	1.6	5.9	2.9
9aB	12.5	8.4	3.8	9.7	9.1	8.6	10.5	9.1	7.2	7.7	1.3	7.9	1.3	7.7	9.2	1.7	5.6	2.6
9bA	11.5	6.5	3.1	8.4	8.3	8.2	10.5	8.4	8.3	—	1.8	—	—	8.2	9.1	1.7	5.7	2.8
9bB	—*	6.6	4.2	8.4	8.6	—*	—*	8.4	7.5	—	1.6	—	—	8.5	9.1	1.7	5.8	2.7
9cA	11.2	6.4	2.9	8.7	8.7	8.2	11.1	8.5	8.2	—	1.7	—	—	8.0	9.1	1.7	5.8	2.9
9cB	12.0	7.8	3.7	—*	9.1	8.0	—*	9.1	7.0	—	1.3	—	—	9.1	9.0	1.4	5.6	2.2
9dA	—*	—*	—*	—*	—*	—*	—*	—*	8.2	—	2.0	—	—	8.7	9.1	1.7	5.7	2.7
9dB	—*	—*	—*	—*	—*	—*	—*	—*	7.1	—	2.0	—	—	9.0	9.1	1.7	5.7	2.8
9eA**	—*	—*	—*	—*	—*	—*	—*	—*	8.3	—	1.5	—	—	9.2	9.0	1.6	5.7	2.7
9eB**	—*	—*	—*	—*	—*	—*	—*	—*	7.1	—	1.5	—	—	9.4	9.0	1.6	5.7	2.8

* The spin-spin coupling constants were not determined.
** $J_{F,7}$ = 5.5 Hz.

1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinolin-9(9a*H*)-one (11bB), (3a*S,9a*S**,11*R**,13a*R**,13b*S**,13c*S**)-5-methoxy-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinolin-9(9a*H*)-one (11cA), (3a*S**,9a*R**,11*S**,13a*S**,13b*S**,13c*S**)-5-methoxy-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinolin-9(9a*H*)-one (11cB), (3a*S**,9a*S**,11*R**,13a*R**,13b*S**,13c*S**)-5-chloro-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinolin-9(9a*H*)-one (11dA), (3a*S**,9a*R**,11*S**,13a*S**,13b*S**,13c*S**)-5-chloro-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinolin-9(9a*H*)-one (11dB), (3a*S**,9a*S**,11*R**,13a*R**,13b*S**,13c*S**)-5-fluoro-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinolin-9(9a*H*)-one (11eA), and (3a*S**,9a*R**,11*S**,13a*S**,13b*S**,13c*S**)-5-fluoro-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinolin-9(9a*H*)-one (11eB) (general procedure).** A solution of tetrahydroquinoline **3a—e** (4.15 mmol, 1.1 mL), acryloyl chloride (12 mmol), and triethylamine (2.4 mL, 16.7 mmol) in benzene (50 mL) was refluxed for 2—4 h (TLC monitoring), cooled, and poured into water (50 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3×40 mL). The organic fractions were combined and dried with magnesium sulfate. After evaporation of the solvent, mixtures of isomers **A** and **B** of furoisoindoloquinolines **11a—e** were obtained as white crystals. The ratios of isomers and spectroscopic characteristics are given in Tables 1, 12, and 13.

(4a*S,10a*S**,11*R**,12*S**,14a*R**,14b*S**,14c*S**)-10-Oxo-2,3,10,10a,11,12,14b,14c-octahydro-1*H*,4a*H*-12,14a-epoxyisoindolo[2,1-*a*]pyrano[3,2-*c*]quinoline-11-carboxylic acid (10A), (4a*S**,10a*R**,11*S**,12*R**,14a*S**,14b*S**,14c*S**)-10-oxo-2,3,10,10a,11,12,14b,14c-octahydro-1*H*,4a*H*-12,14a-epoxyisoindolo[2,1-*a*]pyrano[3,2-*c*]quinoline-11-carboxylic acid (10B), (5*S**,6a*S**,6b*R**,9*S**,10*R**,10a*S**)-5-ethoxy-11-oxo-6,6a,9,10,10a,11-hexahydro-5*H*-6b,9-epoxyisoindolo[2,1-*a*]quinoline-10-carboxylic acid (13A), (5*S**,6a*S**,6b*S**,9*R**,10*S**,10a*R**)-5-ethoxy-11-oxo-6,6a,9,10,10a,11-hexahydro-5*H*-6b,9-epoxyisoindolo[2,1-*a*]quinoline-10-carboxylic acid (13B), (5*S**,6a*S**,6b*R**,9*S**,10*R**,10a*S**)-11-oxo-5-(2-oxopyrrolidin-1-yl)-6,6a,9,10,10a,11-hexahydro-5*H*-6b,9-epoxyisoindolo[2,1-*a*]quinoline-10-carboxylic acid (14A), and (5*S**,6a*S**,6b*S**,9*R**,10*S**,10a*R**)-11-oxo-5-(2-oxopyrrolidin-1-yl)-6,6a,9,10,10a,11-hexahydro-5*H*-6b,9-epoxyisoindolo[2,1-*a*]quinoline-10-carboxylic acid (14B) (general procedure *A*).** A solution of maleic anhydride (0.43 g, 4.36 mmol) in toluene (10 mL) was added to a solution of furyl-substituted amine **4a**, **5**, or **6a** (4.15 mmol) in toluene (10 mL) at 0—3 °C. The reaction mixture was kept at 0—3 °C for 3 days (TLC monitoring). The crystals that formed were filtered off and washed with diethyl ether. Mixtures of isomers **A** and **B** of the corresponding isoindoloquinolinecarboxylic acids **10**, **13**, and **14** were obtained as white crystals. The ratios of isomers and the yields are given in Table 1.

General procedure *B*. A solution of tetrahydroquinoline **4a**, **5**, or **6a** (4.15 mmol) and maleic anhydride (0.43 g, 4.36 mmol) in toluene (20 mL) (for **5** and **6a**) or *o*-xylene (20 mL) (for **4a**) was refluxed for 3 h. The white crystals that precipitated were filtered off. Isoindoloquinolinecarboxylic acids *trans*-**10A**, *cis*-**13B**, and *cis*-**14B** were obtained.

Compound **10A**. MS, *m/z* (I_{rel} (%)): 353 $[M]^+$ (32), 294 (30), 254 (100), 196 (76), 99 (75), 77 (45). ^{1}H NMR (DMSO-d_6), δ: 7.91 (br.d, 1 H, H(8), $J_{7,8}$ = 8.0 Hz); 7.46 (dd, 1 H, H(5), $J_{5,7}$ = 1.0 Hz, $J_{5,6}$ = 7.7 Hz); 7.28 (ddd, 1 H, H(7), $J_{7,8}$ = 8.0 Hz, $J_{6,7}$ = 7.7 Hz, $J_{5,7}$ = 1.0 Hz); 7.18 (dt, 1 H, H(6), $J_{6,7}$ = $J_{5,6}$ = 7.7 Hz, $J_{6,8}$ = 1.0 Hz); 6.88 (d, 1 H, H(14), $J_{13,14}$ = 5.7 Hz); 6.54 (dd, 1 H, H(13), $J_{13,14}$ = 5.7 Hz, $J_{12,13}$ = 1.7 Hz); 5.19 (br.d, 1 H, H(4a), $J_{4a,14c}$ = 6.0 Hz); 5.05 (d, 1 H, H(12), $J_{12,13}$ = 1.7 Hz); 4.35 (d, 1 H, H(14b), $J_{14b,14c}$ = 1.8 Hz); 3.56 (m, 1 H, H(3A)); 3.09 (m, 1 H, H(3B)); 2.94 (d, 1 H, H(11), $J_{10a,11}$ = 9.1 Hz); 2.61 (d, 1 H, H(10a), $J_{10a,11}$ = 9.1 Hz); 2.57 (m, 1 H, H(14c)); 1.70 (m, 2 H, H(2)); 1.47 (m, 1 H, H(1A), $J_{1A,1B}$ = 13.6 Hz); 1.11 (m, 1 H, H(1B), $J_{1A,1B}$ = 13.6 Hz).

Compound **13B**. MS, *m/z* (I_{rel} (%)): 341 $[M]^+$ (5), 242 (25), 167 (20), 130 (52), 93 (100), 77 (60), 65 (45). ^{1}H NMR (DMSO-d_6), δ: 8.57 (dd, 1 H, H(1), $J_{1,2}$ = 8.4 Hz, $J_{1,3}$ = 1.1 Hz); 7.48 (dd, 1 H, H(4), $J_{3,4}$ = 7.6 Hz, $J_{2,4}$ = 1.1 Hz); 7.21 (ddd, 1 H, H(2), $J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 7.6 Hz, $J_{2,4}$ = 1.1 Hz); 7.07 (dt, 1 H, H(3), $J_{1,3}$ = 1.1 Hz, $J_{2,3}$ = $J_{3,4}$ = 7.6 Hz); 6.58 (d, 1 H, H(7), $J_{7,8}$ = 5.7 Hz); 6.51 (dd, 1 H, H(8), $J_{8,9}$ = 1.7 Hz, $J_{7,8}$ = 5.7 Hz); 5.04 (d, 1 H, H(9), $J_{8,9}$ = 1.7 Hz); 4.75 (dd, 1 H, H(5), $J_{5,6ax}$ = 11.4 Hz, $J_{5,6eq}$ = 5.7 Hz); 4.72 (dd, 1 H, H(6a), $J_{6a,6ax}$ = 12.4 Hz, $J_{6a,6eq}$ = 2.4 Hz); 3.71 (dq, 1 H, $OC\underline{H}_AH_BCH_3$, J = 7.0 Hz, J = 9.4 Hz); 3.58 (dq, 1 H, $OCH_A\underline{H}_BCH_3$, J = 7.0 Hz, J = 9.4 Hz); 3.11 (d, 1 H, H(10), $J_{10,10a}$ = 9.2 Hz); 2.57 (d, 1 H, H(10a), $J_{10,10a}$ = 9.2 Hz); 2.44 (ddd, 1 H, H_{eq}(6), $J_{6eq,6ax}$ = 12.4 Hz, $J_{5,6eq}$ = 5.7 Hz, $J_{6a,6eq}$ = 2.4 Hz); 1.69 (dt, 1 H, H_{ax}(6), $J_{6eq,6ax}$ = $J_{6a,6ax}$ = 12.4 Hz, $J_{5,6ax}$ = 11.4 Hz); 1.21 (t, 3 H, $OCH_2C\underline{H}_3$, J = 7.0 Hz).

Compound **14B**. MS, *m/z* (I_{rel} (%)): 380 $[M]^+$ (3), 281 (10), 206 (32), 196 (100), 167 (20), 130 (25), 91 (30), 44 (35). ^{1}H NMR (DMSO-d_6), δ: 8.63 (dd, 1 H, H(1), $J_{1,2}$ = 8.5 Hz, $J_{1,3}$ = 1.1 Hz); 7.24 (ddd, 1 H, H(2), $J_{1,2}$ = 8.5 Hz, $J_{2,3}$ = 7.5 Hz, $J_{2,4}$ = 0.7 Hz); 7.07 (dt, 1 H, H(3), $J_{1,3}$ = 1.1 Hz, $J_{3,4}$ = $J_{2,3}$ = 7.5 Hz); 6.96 (br.d, 1 H, H(4), $J_{3,4}$ = 7.5 Hz); 6.60 (d, 1 H, H(7), $J_{7,8}$ = 5.7 Hz); 6.51 (dd, 1 H, H(8), $J_{8,9}$ = 1.7 Hz, $J_{7,8}$ = 5.7 Hz); 5.48 (br.s, 1 H, H(6a)); 5.04 (d, 1 H, H(9), $J_{8,9}$ = 1.7 Hz); 4.87 (dd, 1 H, H(5), $J_{5,6ax}$ = 11.5 Hz, $J_{5,6eq}$ = 3.1 Hz); 3.19—3.28 (m, 2 H, H(5′A), H_{ax}(6)); 3.13 (d, 1 H, H(10), $J_{10,10a}$ = 9.1 Hz); 2.94 (m, 1 H, H(5′B)); 2.58 (d, 1 H, H(10a), $J_{10,10a}$ = 9.1 Hz); 2.36 (m, 2 H, H(3′)); 1.95 (m, 2 H, H(4′), H_{eq}(6)).

(4a*S,10a*S**,12*R**,14a*R**,14b*S**,14c*S**)-2,3,11,12,14b,14c-Hexahydro-1*H*,4a*H*-12,14a-epoxyisoindolo[2,1-*a*]pyrano[3,2-*c*]quinolin-10(10a*H*)-one (12A), (4a*S**,10a*R**,12*S**,14a*S**,14b*S**,14c*S**)-2,3,11,12,14b,14c-hexahydro-1*H*,4a*H*-12,14a-epoxyisoindolo[2,1-*a*]pyrano[3,2-*c*]quinolin-10(10a*H*)-one (12B), (5*S**,6a*S**,6b*S**,9*S**,10a*R**)-5-ethoxy-6,6a,10,10a-tetrahydro-5*H*-6b,9-epoxyisoindolo[2,1-*a*]quinolin-11(9*H*)-one (15B), and (5*S**,6a*S**,6b*S**,9*S**,10a*R**)-5-(2-oxopyrrolidin-1-yl)-6,6a,10,10a-tetrahydro-5*H*-6b,9-epoxyisoindolo[2,1-*a*]quinolin-11(9*H*)-one (16B) (general procedure).** A solution of amine **4a**, **5**, or **6a** (4.15 mmol, 1.1 mL), acryloyl chloride (12 mmol), and triethylamine (2.3 mL, 16.7 mmol) in benzene (50 mL) was refluxed for 2 h. Then the reaction mixture was poured into water (50 mL), the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3×40 mL). The organic fractions were combined and dried with magnesium sulfate. After

Table 12. Chemical shifts (δ) of protons in the ^{1}H NMR spectra of compounds **11a—e** and **17—19** in $CDCl_3$

Compound	δ																	
	H(1A) (m)	H(1B) (m)	H(2A)	H(2B)	H(3a) (d)	H(4)	H(5)	H(6)	H(7)	H(9a)	H(10) *endo*	H(10) *exo*	H(11)	H(12) (dd)	H(13)	H(13b)	H(13c)	Other protons
11aA	2.06	1.88	3.85 (m)	3.62 (ddd)	5.38	7.42 (dd)	7.16 (dt)	7.31 (ddd)	8.04 (dd)	2.62 (dd)	1.72 (dd)	2.33 (ddd)	5.14 (dd)	6.49	6.45 (br.d)	4.46 (d)	3.14 (m)	—
11aB	2.13	1.88	3.85 (q)	3.66 (ddd)	5.26	7.49 (dd)	7.12 (dt)	7.27 (ddd)	8.66 (dd)	2.64 (dd)	1.63 (dd)	2.28 (ddd)	5.13 (dd)	6.48	6.53 (d)	4.77 (d)	2.91 (m)	—
11bA	2.06	1.76	3.81 (m)	3.62 (m)	5.32	7.23 (d)	—	7.21 (dd)	7.91 (d)	2.63 (dd)	1.72 (dd)	2.32 (ddd)	5.14 (dd)	6.49	6.45 (d)	4.43 (d)	3.12 (m)	2.26 (s, Me)
11bB	2.13	1.92	3.92 (m)	3.78 (m)	5.22	7.28 (d)	—	7.02 (dd)	8.57 (d)	2.64 (dd)	1.63 (dd)	2.26 (ddd)	5.13 (dd)	6.48	6.53 (d)	4.77 (d)	2.91 (m)	2.26 (s, Me)
11cA	2.04	1.85	3.92—3.66 (m)		5.32	7.26 (s)	—	7.14 (dd)	7.93 (d)	2.62 (dd)	1.73 (dd)	2.32 (ddd)	5.14 (dd)	6.49	6.45 (d)	4.43 (d)	3.12 (m)	3.79 (s, OMe)
11cB	2.14	1.85	3.92—3.66 (m)		5.21	7.36 (s)	—	7.00 (br.d)	8.60 (d)	2.63 (dd)	1.63 (dd)	2.26 (ddd)	5.13 (dd)	6.48	6.54 (d)	4.74 (d)	2.89 (m)	3.85 (s, OMe)
11dA	2.05	1.83	3.91 (m)	3.69 (ddd)	5.31	7.41 (br.d)	—	7.26 (dd)	7.99 (d)	2.62 (dd)	1.72 (dd)	2.32 (ddd)	5.14 (dd)	6.49	6.45 (d)	4.45 (d)	2.89 (m)	—
11dB	2.13	1.83	3.94 (dt)	3.86 (q)	5.19	7.46 (br.d)	—	7.21 (dd)	8.63 (d)	2.64 (dd)	1.64 (dd)	2.26 (ddd)	5.13 (dd)	6.48	6.53 (d)	4.77 (d)	2.89 (m)	—
11eA	2.05	1.75	3.95—3.65 (m)		5.31	7.13 (dd)	—	6.94 (m)	8.00 (dd)	2.62 (dd)	1.72 (dd)	2.32 (ddd)	5.14 (dd)	6.49	6.45 (d)	4.45 (d)	3.19 (m)	—
11eB	2.14	1.75	3.95—3.65 (m)		5.19	7.17 (dd)	—	7.03 (m)	8.67 (dd)	2.65 (dd)	1.63 (dd)	2.26 (ddd)	5.12 (dd)	6.48	6.53 (d)	4.77 (d)	3.12 (m)	—
17A	2.04	1.81	3.92 (dt)	3.89 (dt)	5.37	7.42 (dd)	7.17 (dt)	7.29 (dt)	7.97 (dd)	2.86 (d)	2.96 (d)	—	5.22 (d)	6.55	6.66 (d)	4.55 (d)	3.14 (ddt)	3.84 (s, OMe)
17B	2.22	2.01	3.86 (q)	3.65 (dt)	5.26	7.49 (d)	7.13 (t)	7.25 (t)	8.60 (d)	2.79 (d)	3.00 (d)	—	5.23 (s)	6.52	6.58 (d)	4.75 (s)	2.92 (m)	3.81 (s, OMe)
18A	2.03	1.81	3.91 (dt)	3.85 (dt)	5.36	7.41 (dd)	7.16 (dt)	7.28 (dt)	7.96 (dd)	2.94 (d)	2.83 (d)	—	5.20 (d)	6.53	6.64 (d)	4.54 (d)	3.12 (ddt)	4.34—4.26 (m, OCH_2); 1.34 (t, Me)
18B	2.23	2.03	3.85 (q)	3.64 (ddd)	5.26	7.48 (br.d)	7.12 (dt)	7.24 (ddd)	8.61 (dd)	2.99 (d)	2.77 (d)	—	5.22 (d)	6.51	6.57 (d)	4.75 (d)	2.91 (m)	4.25 (m, OCH_2); 1.34 (t, Me)
19A	2.06	1.84	3.94 (dt)	3.87 (dt)	5.39	7.44 (br.d)	7.19 (br.t)	7.31 (br.t)	8.00 (br.d)	2.82 (d)	2.95 (d)	—	5.21 (d)	6.56	6.67 (d)	4.57 (d)	3.15 (m)	5.20 (sept, OCH); 1.38, 1.34 (both d, Me)
19B	2.23	2.05	3.87 (q)	3.66 (dt)	5.28	7.50 (d)	7.13 (dt)	7.26 (ddd)	8.66 (dd)	2.98 (d)	2.74 (d)	—	5.21 (d)	6.52	6.59 (d)	4.75 (d)	2.93 (m)	5.13 (sept, OCH); 1.36, 1.27 (both d, Me)

Table 13. Spin-spin coupling constants (J) of protons in the ^{1}H NMR spectra of compounds **11a—e** and **17—19** in $CDCl_3$

Compound	J/Hz													
	3a, 13c	4, 5	4, 6	5, 6	5, 7	6, 7	13b, 13c	9a, 10_{exo}	9a, 10_{endo}	10_{exo}, 10_{endo}	10_{exo}, 11	11, 12	12, 13	Other coupling constants
11aA	7.0	7.7	1.1	7.7	1.1	8.5	2.6	3.6	8.7	11.8	4.5	1.5	5.8	—
11aB	8.1	7.7	—	7.7	—	8.3	2.7	3.9	8.9	11.8	4.5	1.5	5.8	—
11bA	7.0	—	1.8	—	—	8.5	4.7	3.5	8.8	12.0	4.7	1.3	5.8	—
11bB	8.0	—	1.8	—	—	8.5	2.5	3.5	8.7	11.7	4.5	1.5	5.8	—
11cA	7.1	—	2.6	—	—	9.2	2.6	3.6	8.7	11.8	4.5	1.6	5.8	—
11cB	8.1	—	2.6	—	—	9.0	2.8	3.8	8.9	11.8	4.5	1.6	5.8	—
11dA	7.1	—	2.5	—	—	9.0	2.6	3.5	8.8	11.9	4.6	1.6	5.8	—
11dB	8.2	—	2.5	—	—	8.8	2.8	3.8	8.9	11.9	4.7	1.6	5.8	—
11eA	7.0	—	3.0	—	—	9.2	2.6	3.5	8.7	11.8	4.6	1.5	5.8	$J_{F,7} = 5.2$, $J_{F,4} = 8.0$
11eB	8.1	—	3.0	—	—	9.1	2.7	3.8	9.0	11.8	4.4	1.6	5.8	$J_{F,7} = 5.1$, $J_{F,4} = 8.6$
17A	8.2	7.7	1.3	7.7	1.3	7.7	2.7	—	9.1	—	—	1.7	5.9	$J_{2A,2B} = 8.3$, $J_{2A,1B} = 8.6$
17B	7.1	7.8	—	7.7	—	8.4	2.5	—	8.9	—	—		5.7	$J_{2A,2B} = 8.5$
18A	8.2	7.7	1.5	7.8	1.2	7.8	2.8	—	9.1	—	—	1.7	5.8	$J_{2A,2B} = 8.5$, $J_{2A,1B} = 8.5$
18B	7.2	7.5	1.1	8.4	1.0	7.5	2.5	—	9.0	—	—	1.7	5.7	$J_{2A,2B} = 8.5$, $J_{2A,1B} = 8.5$
19A	8.3	7.7	—*	7.7	—*	8.5	2.6	—	9.0	—	—	1.5	5.8	$J_{CH,Me} = 6.3$
19B	7.1	7.6	1.0	7.6	1.0	8.4	2.4	—	8.9	—	—	1.6	5.7	$J_{CH,Me} = 6.3$

* The spin-spin coupling constants were not determined.

evaporation of the solvent, isoindoloquinolines **12**, **15B**, and **16B** were obtained as white crystals. The ratios of isomers and the yields are given in Table 1.

Compound **12A**. ^{1}H NMR ($CDCl_3$), δ: 8.17 (dd, 1 H, H(8), $J_{6,8}$ = 1.0 Hz, $J_{7,8}$ = 8.0 Hz); 7.58 (br.d, 1 H, H(5), $J_{5,6}$ = 7.7 Hz); 7.31 (br.t, 1 H, H(7), $J_{7,8}$ = 8.0 Hz, $J_{6,7}$ = 7.7 Hz); 7.19 (dt, 1 H, H(6), $J_{6,8}$ = 1.0 Hz, $J_{6,7}$ = $J_{5,6}$ = 7.7 Hz); 6.57 (d, 1 H, H(14), $J_{13,14}$ = 5.7 Hz); 6.49 (dd, 1 H, H(13), $J_{12,13}$ = 1.7 Hz, $J_{13,14}$ = 5.7 Hz); 5.17 (br.d, 1 H, H(4a), $J_{4a,14c}$ = 6.3 Hz); 5.12 (dd, 1 H, H(12), $J_{12,13}$ = 1.7 Hz, $J_{12,11exo}$ = 4.5 Hz); 4.30 (d, 1 H, H(14b), $J_{14b,14c}$ = 2.0 Hz); 3.67 (m, 1 H, H(3A)); 3.31 (dt, 1 H, H(3B), J = 2.0 Hz, J = 12.4 Hz); 2.60 (m, 1 H, H(14c)); 2.54 (dd, 1 H, H(10a), $J_{10a,11exo}$ = 3.7 Hz, $J_{10a,11endo}$ = 9.1 Hz); 2.32 (ddd, 1 H, H(11)$_{exo}$, $J_{10a,11exo}$ = 3.7 Hz, $J_{11exo,12}$ = 4.5 Hz, $J_{11exo,11endo}$ = 11.7 Hz); 2.20 (m, 1 H, H(2A)); 1.84 (m, 1 H, H(2B)); 1.72 (dd, 1 H, H(11)$_{endo}$, $J_{10a,11endo}$ = 9.1 Hz, $J_{11exo,11endo}$ = 11.7 Hz); 1.67 (m, 1 H, H(1A)); 1.52 (m, 1 H, H(1B)).

Compound **12B**. MS, m/z (I_{rel} (%)): 309 $[M]^+$ (52), 250 (23), 196 (100), 158 (20), 77 (22), 55 (63). ^{1}H NMR ($CDCl_3$), δ: 8.83 (d, 1 H, H(8), $J_{7,8}$ = 8.3 Hz); 7.55 (d, 1 H, H(5), $J_{5,6}$ = 7.7 Hz); 7.29 (dd, 1 H, H(7), $J_{7,8}$ = 8.3 Hz, $J_{6,7}$ = 7.7 Hz); 7.14 (t, 1 H, H(6), $J_{6,7}$ = $J_{5,6}$ = 7.7 Hz); 6.47 (dd, 1 H, H(13), $J_{12,13}$ = 1.7 Hz, $J_{13,14}$ = 5.7 Hz); 6.45 (d, 1 H, H(14), $J_{13,14}$ = 5.7 Hz); 5.14 (d, 1 H, H(4a), $J_{4a,14c}$ = 6.3 Hz); 5.12 (dd, 1 H, H(12), $J_{12,13}$ = 1.7 Hz, $J_{12,11exo}$ = 4.5 Hz); 4.49 (d, 1 H, H(14b), $J_{14b,14c}$ = 2.4 Hz); 3.59 (br.dd, 1 H, H(3A), J = 4.7 Hz, J = 11.3 Hz); 3.36 (dt, 1 H, H(3B), J = 2.3 Hz, J = 11.3 Hz); 2.61 (m, 1 H, H(14c)); 2.58 (dd, 1 H, H(10a), $J_{10a,11exo}$ = 3.3 Hz, $J_{10a,11endo}$ = 8.6 Hz); 2.24 (ddd, 1 H, H(11)$_{exo}$, $J_{10a,11exo}$ = 3.2 Hz, $J_{11exo,12}$ = 4.5 Hz, $J_{11exo,11endo}$ = 11.8 Hz); 2.21 (m, 1 H, H(2A)); 1.68 (m, 1 H, H(2B)); 1.59 (dd, 1 H, H(11)$_{endo}$, $J_{10a,11endo}$ = 8.6 Hz, $J_{11exo,11endo}$ = 11.8 Hz); 1.41 (br.d, 1 H, H(1A), J = 13.3 Hz); 1.30 (dq, 1 H, H(1B), J = 3.7 Hz, J = 13.3 Hz).

Compound **15B**. MS, m/z (I_{rel} (%)): 297 $[M]^+$ (82), 196 (100), 167 (15), 77(20), 55 (60). ^{1}H NMR ($CDCl_3$), δ: 8.69 (dd, 1 H, H(1), $J_{1,2}$ = 8.1 Hz, $J_{1,3}$ = 1.0 Hz); 7.57 (dd, 1 H, H(4), $J_{3,4}$ = 7.7 Hz, $J_{2,4}$ = 0.9 Hz); 7.26 (ddd, 1 H, H(2), $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 7.7 Hz, $J_{2,4}$ = 0.9 Hz); 7.10 (dt, 1 H, H(3), $J_{1,3}$ = 1.0 Hz, $J_{2,3}$ = $J_{3,4}$ = 7.7 Hz); 6.58 (d, 1 H, H(7), $J_{7,8}$ = 5.6 Hz); 6.48 (dd, 1 H, H(8), $J_{8,9}$ = 1.6 Hz, $J_{7,8}$ = 5.6 Hz); 5.11 (dd, 1 H, H(9), $J_{8,9}$ = 1.6 Hz, $J_{9,10endo}$ = 4.5 Hz); 4.78 (dd, 1 H, H(5), $J_{5,6ax}$ = 11.6 Hz, $J_{5,6eq}$ = 5.7 Hz); 4.53 (dd, 1 H, H(6a), $J_{6a,6ax}$ = 12.6 Hz, $J_{6a,6eq}$ = 2.4 Hz); 3.72 (dq, 1 H, OC$\underline{H}_A$H$_B$CH$_3$, J = 7.0 Hz, J = 16.0 Hz); 3.58 (dq, 1 H, OCH$_A\underline{H}_B$CH$_3$, J = 7.0 Hz, J = 16.0 Hz); 2.63 (dd, 1 H, H(10a), $J_{10a,10exo}$ = 3.3 Hz, $J_{10a,10endo}$ = 8.8 Hz); 2.47 (ddd, 1 H, H$_{eq}$(6), $J_{6eq,6ax}$ = 12.7 Hz, $J_{5,6eq}$ = 5.7 Hz, $J_{6a,6eq}$ = 2.4 Hz); 2.28 (ddd, 1 H, H(10)$_{exo}$, $J_{10a,10exo}$ = 3.3 Hz, $J_{10exo,9}$ = 4.5 Hz, $J_{10exo,10endo}$ = 11.9 Hz); 2.09 (dq, 1 H, H$_{ax}$(6), $J_{6eq,6ax}$ = $J_{6a,6ax}$ = 12.6 Hz, $J_{5,6ax}$ = 11.6 Hz); 1.65 (dd, 1 H, H(10)$_{endo}$, $J_{10a,10endo}$ = 8.8 Hz, $J_{10exo,10endo}$ = 11.9 Hz); 1.29 (t, 3 H, OCH$_2$C$\underline{H}_3$, J = 7.0 Hz).

Compound **16B**. MS, m/z (I_{rel} (%)): 336 $[M]^+$ (20), 251 (90), 196 (100), 167 (25), 130 (30), 55 (65). ^{1}H NMR ($CDCl_3$), δ: 8.71 (dd, 1 H, H(1), $J_{1,2}$ = 8.3 Hz, $J_{1,3}$ = 0.8 Hz); 7.27 (dd, 1 H, H(2), $J_{1,2}$ = 8.3 Hz, $J_{2,3}$ = 7.7 Hz); 7.07 (dt, 1 H, H(3), $J_{1,3}$ = 0.8 Hz, $J_{2,3}$ = $J_{3,4}$ = 7.7 Hz); 6.99 (br.d, 1 H, H(4), $J_{3,4}$ = 7.7 Hz); 6.48 (dd, 1 H, H(8), $J_{8,9}$ = 1.5 Hz, $J_{7,8}$ = 5.8 Hz); 6.42 (d, 1 H, H(7), $J_{7,8}$ = 5.8 Hz); 5.68 (dd, 1 H, H(5), $J_{5,6ax}$ = 11.1 Hz, $J_{5,6eq}$ = 7.0 Hz); 5.11 (dd, 1 H, H(9), $J_{8,9}$ = 1.5 Hz, $J_{9,10exo}$ = 4.5 Hz); 4.64 (dd, 1 H, H(6a), $J_{6a,6eq}$ = 4.9 Hz, $J_{6a,6ax}$ = 10.7 Hz); 3.22 (dt, 1 H, H(5′A), J = 7.6 Hz, J = 9.7 Hz); 3.09 (dt, 1 H, H(5′B), J = 6.2 Hz, J = 9.7 Hz); 2.67 (d, 1 H, H(10a), $J_{10exo,10a}$ = 3.3 Hz, $J_{10endo,10a}$ = 8.7 Hz); 2.50 (m, 2 H, H(3′)); 2.29 (ddd, 1 H, H(10)$_{exo}$, $J_{10exo,10a}$ = 3.3 Hz, $J_{10exo,10endo}$ = 11.9 Hz, $J_{10exo,9}$ = 4.5 Hz); 2.22—2.16 (m, 2 H, H(6)); 2.02 (m, 2 H, H(4′)); 1.67 (dd, 1 H, H(10)$_{endo}$, $J_{10endo,10a}$ = 8.7 Hz, $J_{10exo,10endo}$ = 11.9 Hz).

Methyl (17), ethyl (18), and isopropyl (19) (3a*S,9a*S**,10*R**,11*S**,13a*R**,13b*S**,13c*S**)- and (3a*S**,9a*R**,10*S**,11*R**,13a*S**,13b*S**,13c*S**)-9-oxo-1,2,9,9a,10,11,13b,13c-octahydro-3a*H*-11,13a-epoxyfuro[3,2-*c*]isoindolo[2,1-*a*]quinoline-10-carboxylates (isomers A and B).** Furoisoindoloquinolinecarboxylic acid **9aA** (1.50 g, 4.42 mmol) was refluxed in 30 mL of methanol (for **17**), ethanol (for **18**), or isopropyl alcohol (for **19**) in the presence of one drop of H_2SO_4 for 2—6 h. Then the reaction mixture was poured into water (50 mL) and extracted with chloroform (3×50 mL). The extracts were dried with magnesium sulfate, the solvent was evaporated, and white crystals of esters **17—19** were obtained. The ratios of isomer and the yields are presented in Scheme 5. The ^{1}H NMR spectroscopic data are given in Tables 12 and 13.

Compound **17A**. ^{13}C NMR ($CDCl_3$), δ: 25.1 (C(1)); 39.7 (C(13c)); 45.2 (C(10)); 51.8 (C(9a)); 52.3 ($CO_2\underline{Me}$); 58.8 (C(13b)); 67.5 (C(2)); 77.3 (C(3a)); 81.3 (C(11)); 89.9 (C(13a)); 121.2 (C(7)); 125.4 (C(6)); 127.4 (C(3b)); 128.4 (C(5)); 129.6 (C(4)); 134.0 (C(12)); 135.0 (C(7a)); 137.6 (C(13)); 168.5 (O—C=O); 171.8 (C(9)).

Compound **17B**. ^{13}C NMR ($CDCl_3$), δ: 24.9 (C(1)); 38.6 (C(13c)); 44.6 (C(10)); 52.7 (C(9a)); 52.2 ($CO_2\underline{Me}$); 56.2 (C(13b)); 67.0 (C(2)); 67.0 (C(3a)); 81.6 (C(11)); 89.7 (C(13a)); 117.9 (C(7)); 124.3 (C(6)); 126.1 (C(3b)); 128.4 (C(5)); 129.4 (C(4)); 135.2 (C(12)); 135.6 (C(7a)); 137.4 (C(13)); 169.8 (O—C=O); 171.8 (C(9)).

X-ray diffraction study. The molecular structures of **17A** and **17B** were determined on an Enraf-Nonius CAD-4 three-circle diffractometer at 293 K (λ(Mo-Kα), graphite monochromator, ω-scanning technique, θ/2θ = 60°, λ = 0.71073 Å). The structures were solved by direct methods using the SHELXS-97 program package[18] and refined anisotropically by the least-squares method using the SHELXL-97 program package.[19] The complete crystallographic data were deposited with the Cambridge Structural Database (CCDC 252721 for **17A** and 607604 for **17B**). The structures and the atomic numbering schemes are presented in Figs 1 and 2, respectively.

Compound **17A**. Single crystals were grown by crystallization from an AcOEt—$CHCl_3$ mixture. The crystal dimensions were 0.42×0.22×0.12 mm, colorless rhombus-shaped crystals, $C_{20}H_{19}NO_5$, M = 353.36, space group $P2_1/c$, monoclinic system, a = 11.128(2) Å, b = 18.295(4) Å, c = 8.3280(17) Å, β = 107.04(3)°, V = 1621.0(6) Å^3, Z = 4, d_{calc} = 1.448 g cm^{-3}, μ = 0.105 mm^{-1}, the number of measured reflections was 4334, the number of reflections with $I \geq 2\sigma(I)$ was 2148, the number of parameters in the refinement was 235, $R_1(I \geq 2\sigma(I))$ = 0.0594, wR_2 = 0.1608, S = 0.979.

Compound **17B**. Single crystals were grown by crystallization from an AcOEt—hexane mixture. The crystal dimensions were 0.33×0.28×0.19 mm, colorless prisms, $C_{20}H_{19}NO_5$, M = 353.36, space group $P\bar{1}$, triclinic system, a = 10.774(2) Å, b = 12.978(3) Å, c = 13.228(3) Å, α = 71.55(3)°, β = 70.99(3)°, γ = 85.97(3)°, V = 1657.7(6) Å^3, Z = 4, d_{calc} = 1.416 g cm^{-3}, μ = 0.102 mm^{-1}, the number of measured reflections was 6137,

the number of reflections with $I \geq 2\sigma(I)$ was 3568, the number of parameters in the refinement was 470, $R_1(I \geq 2\sigma(I)) = 0.0326$, $wR_2 = 0.0901$, $S = 1.067$.

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