N-Trifluoroacetyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline ozonides

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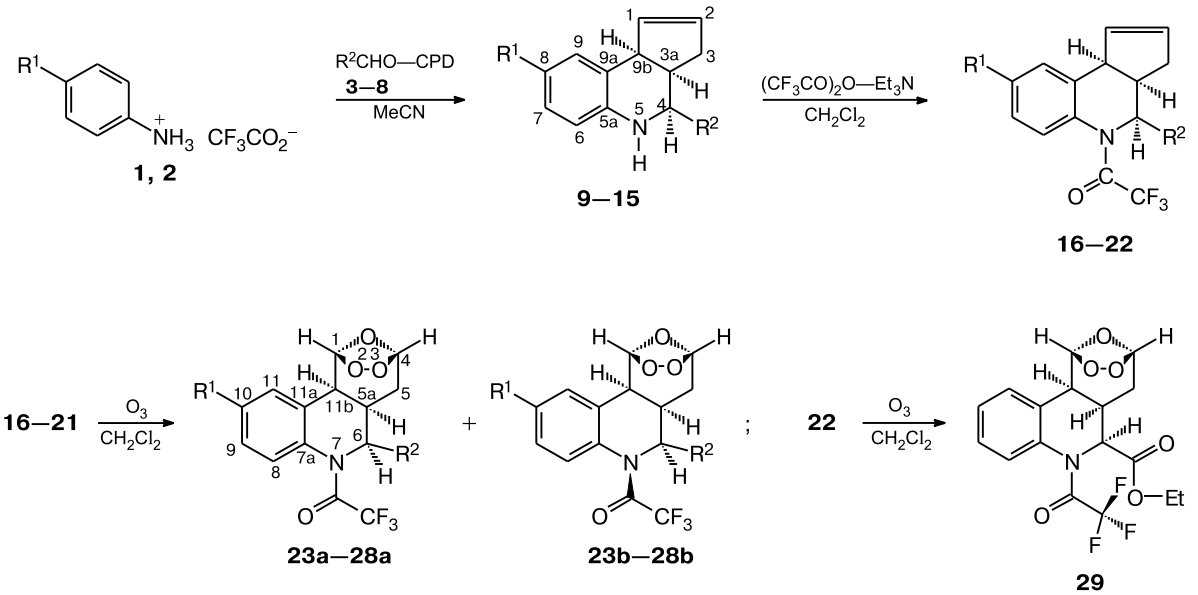
A three-component condensation of aromatic amine, aldehyde, and cyclopentadiene with subsequent *N*-trifluoroacetylation leads to 4- and 4,8-substituted *N*-trifluoroacetyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolines. Ozonation of the double bond in the latter produced the corresponding isomeric stable ozonides having (1*R**,4*S**,5a*R**,6*S**,11b*R**)-configuration and differing in inversion at the carboxamide nitrogen atom.

Key words: cycloaddition, cyclopentadiene, imines, 3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolines, trifluoroacetamides, ozonolysis, ozonides, the Povarov reaction.

Valuable therapeutic properties of natural peroxides produce an increased interest to the chemistry and pharmacology of their synthetic analogs.[1—3] High antimalaria activity of sesquiterpene lactone of artemisinine containing a peroxide bond in the form of 1,2,4-trioxane heterocycle[4] stimulated a search for similar activity in its derivatives,[5] partially synthetic analogs,[6] and synthetic antimalaria peroxides[7] and ozonides.[8—10] To improve antimalaria and biopharmacological properties of synthetic peroxides and ozonides, their conjugates containing weakly basic functional groups and heterocycles were obtained.[11—19]

We have reported the synthesis of *N*-acetyl- and *N*-trifluoroacetyl-4-phenyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline ozonides.[20] In the present work, we described a number of new ozonides of tetrahydroquinolines annulated with cyclopentene, studied their stereochemistry, and found how their conformational state depends on the nature of substituents at positions 4 and 8 of the starting compounds (Scheme 1).

Scheme 1



R^1 = H (**1**, **9**—**13**, **16**—**20**, **23**—**27**), CO_2Me (**2**, **14**, **21**, **28**); R^2 = Ph (**3**, **9**, **14**, **16**, **21**, **23**, **28**), 3-ClC_6H_4 (**4**, **10**, **17**, **24**), 4-ClC_6H_4 (**5**, **11**, **18**, **25**), 4-$F_3CC_6H_4$ (**6**, **12**, **19**, **26**), 4-MeC_6H_4 (**7**, **13**, **20**, **27**), CO_2Et (**8**, **15**, **22**, **29**)

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Substituted 3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]-quinolines **9—15** were obtained by the Povarov reaction.[21] Two approaches to their synthesis were tried: a [4+2] cycloaddition of cyclopentadiene (CPD) to aromatic imines (Schiff bases) and a three-component condensation of an aromatic amine, aldehyde, and CPD using different solvents (acetonitrile, 2,2,2-trifluoroethanol) and catalysts (trifluoroacetic and sulfanilic acids, copper and ytterbium triflates).[21] The best results (high yields and purity of adducts **9—15**) provided a *one-pot* three-component reaction of arylammonium trifluoroacetate **1** or **2** generated *in situ* with an equimolar amount of the corresponding aldehyde **3—8** and a five-fold excess of CPD in MeCN. Treatment of adducts **9—15** with trifluoroacetic anhydride in CH_2Cl_2 in the presence of Et_3N gave rise to the corresponding trifluoroacetamides **16—22**. Ozonolysis of compounds **16—22** in CH_2Cl_2 at 0 °C led to the target ozonides **23—29** (see Scheme 1).

Relative *cis*-orientation of protons at the chiral atom C(3a), C(4), and C(9b) in the molecules of compounds **9—15** and their trifluoroacetamides **16—22** was inferred from the spin-spin coupling constant values of vicinal protons H(3a)—H(9b) ($J_{H(9b),H(3a)}$ = 8.0—9.6 Hz) and H(3a)—H(4) ($J_{H(4),H(3a)}$ = 2.4—8.8 Hz) found from the ^{1}H NMR spectra recorded at −10 °C. Structure **9** was also confirmed by the X-ray diffraction data.[22]

Broad signals for the atoms C(1), C(2) (δ 130.0—135.9), and C(4) (δ 57.4—59.2) of compounds **16—22** in the ^{13}C NMR spectra and the protons at these atoms in the ^{1}H NMR spectra (δ 4.7—6.5) (Table 1) indicate a slow inversion of the heterocycle in the NMR time scale (between conformers with the pseudoaxial and pseudoequatorial C(4)-aryl group) and inversion at the N atom of the heterocycle. At the same time, in the ^{1}H and ^{13}C NMR spectra of the corresponding nonacylated adducts **9—15** the signals indicated are narrow, *i.e.*, exchange between

Table 1. The ^{1}H and ^{13}C NMR spectra (δ, *J*/Hz) of *N*-trifluoroacetamides **17—22**

Group or atom*	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
	Compound **17**		Compound **18**		Compound **19**	
C(1)H	132.24 (br.s)	6.18 (br.s)	130.32 (br.s)	6.17 (br.s)	130.32 (br.s)	6.53 (br.s)
C(2)H	130.74 (br.s)	5.79 (br.s)	130.00 (br.s)	5.77 (br.s)	130.00 (br.s)	5.96 (br.s)
C(3)H_2	35.65	2.08 (d, *J* = 16); 2.64 (br.s)	35.63	2.07 (d, *J* = 15); 2.65 (br.s)	35.63	2.06 (d, *J* = 16); 2.66 (br.s.)
C(3a)H	40.33	3.58 (br.s)	40.14	3.60 (br.s)	45.21	3.67 (br.s)
C(4)H	58.49 (br.s)	6.18 (br.s)	58.25 (br.s)	6.17 (br.s)	58.49 (br.s)	6.53 (br.s)
C(5a)	137.91	—	134.38	—	139.94	—
C(6)H—C(9)H	126.68, 127.11, 129.11	6.69 (d, *J* = 8); 6.98 (t, *J* = 8); 7.33 (t, *J* = 8); 7.45 (d, *J* = 8)	126.66, 127.05, 128.12	7.16—7.44 (m)	124.84, 126.75, 127.18	6.98 (m); 7.57 (m)
C(9a)	125.91 (br.s)	—	125.96 (br.s)	—	133.93	—
C(9b)H	46.53	4.17 (d, *J* = 8)	45.24	4.14 (d, *J* = 9.6)	40.20	4.20 (d, *J* = 8)
C(1′)	133.98	—	134.06	—	139.94	—
C(2′)H	127.11	7.15 (m)	132.24	6.77 (d, *J* = 8.4)	129.49	7.33 (m)
C(3′)H	—	—	128.12	7.03 (d, *J* = 8.4)	129.49	7.17 (m)
C(3′)	133.77	—	—	—	—	—
C(4′)H	127.92	7.15 (m)	—	—	—	—
C(4′)	—	—	133.92	—	127.93	—
C(5′)H	129.48	6.90 (m)	128.12	7.03 (d, *J* = 8.4)	129.49	7.33 (m)
C(6′)H	128.24	6.90 (m)	130.53	6.77 (d, *J* = 8.4)	124.84	7.33 (m)
C(4′)$\underline{C}F_3$	—	—	—	—	113.98 (q, $^1J_{CF}$ = 280.5)	—
$COCF_3$	155.42 (C=O); 116.68 (q, CF_3, $^1J_{CF}$ = 288.7)	—	156.00 (C=O); 116.67 (q, CF_3, $^1J_{CF}$ = 288.5)	—	155.71 (C=O); 116.67 (q, CF_3, $^1J_{CF}$ = 289.3)	—

(*to be continued*)

Table 1 (*continued*)

Group or atom*	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
	Compound **20**		Compound **21**		Compound **22**	
C(1)H	135.86	6.20 (br.s)	132.30	6.22 (br.s)	132.68 (br.s)	5.91 (br.s)
C(2)H	134.38	5.76 (br.s)	130.50	5.76 (br.s)	131.15 (br.s)	5.83 (br.s)
$C(3)H_2$	35.85	2.63 (m); 2.42 (s); 2.34 (s)	35.86	1.74 (br.s); 2.67 (d.d, J = 10.4, J = 16.4)	35.25	2.71 (m)
C(3a)H	40.53	3.71 (br.s)	40.20	3.65 (m)	41.31	3.28 (m)
C(4)H	59.07	6.20 (br.s)	59.24	5.76 (br.s)	57.36	4.11 (m)
C(5a)	137.56	—	138.41	—	135.28	—
C(6)H—C(9)H	126.44, 127.67, 128.76	6.53—7.48 (m)	127.77, 128.05, 128.23, 129.05	6.83 (d, J = 8); 7.83 (d, J = 8); 8.15 (s)	124.80, 126.42, 127.95	7.29 (m)
C(9a)	125.89	—	125.99	—	124.80	—
C(9b)H	45.36	4.18 (d, J = 8.8)	45.29	4.21 (d, J = 8)	45.25	4.00 (m)
C(1´)	130.47	—	135.62	—	—	—
C(2´)H	127.67	—	128.05	7.06 (d, J = 8)	—	—
C(3´)H	129.16	—	129.05	7.15 (t, J = 8)	—	—
C(4´)H	—	5.43—7.48 (m)	128.54	6.83 (d, J = 8)	—	—
C(4´)	128.63	—	—	—	—	—
C(5´)H	129.94	—	129.05	7.15 (t, J = 8)	—	—
C(6´)H	129.45	—	128.05	7.06 (d, J = 8)	—	—
C(4´)Me	21.26	2.19 (s)	—	—	—	—
$COCF_3$	155.79 (q, C=O, $^2J_{CF}$ = 36); 116.61 (q, CF_3, $^1J_{CF}$ = 283)	—	155.29 (m, C=O); 116.60 (q, CF_3, $^1J_{CF}$ = 288.8)	—	155.90 (m, C=O); 116.54 (q, CF_3, $^1J_{CF}$ = 288.4)	—
8-CO_2Me	—	—	166.40 (C=O); 52.29 (MeO)	3.95 (s, MeO)	—	—
4-CO_2Et	—	—	—	—	168.10 (C=O); 61.38 (CH_2); 13.80 (Me)	4.00 (m, CH_2); 1.11 (t, Me, J = 7)

* The atoms C(1´)—C(6´) are from the aryl group.

the conformers in the molecules of these compounds is rapid, which is slowed down after introduction of the *N*-trifluoroacetyl group.[23]

In the ^{13}C NMR spectra of compounds **16—22** recorded at elevated temperature (+55 °C), the signals for the atoms C(1), C(2), and C(4) become narrow, that evidences an increase in the rate of inversion at the N atom. Similar changes in the character of signals for the protons H(1) and H(2) are observed in the ^1H NMR spectra, however, the signal for the proton H(4) remains broadened, that is due to the higher barrier of the ring inversion.[24]

Ozonation of compounds **16—22** in CH_2Cl_2 at 0 °C occurs at the C(1)—C(2) endocyclic double bond and leads to the corresponding ozonides **23—29** (the synthesis and characteristics of ozonide **23** have been described earlier[20]). The presence of 1,2,4-trioxolane ring in the ozonides was confirmed by the presence of narrow signals in their ^{13}C NMR spectra (Table 2) in the region characteristic of ozonides[20,25] δ 98.9—101.5 (C(1) and C(4)) instead of broad signals for the atoms C(1) and C(2) in the spectra of the starting compounds (δ 130.0—135.9). As it has been noted earlier[20] for ozonide **23**, double sets of signals are observed in the ^1H and ^{13}C NMR spectra of compounds **24—28** with an aryl group at position 6, that evidences formation of a mixture of two ozonides: with pseudoaxial (conformers **a**) and pseudoequatorial (conformers **b**) position of the aryl group. Proportion of conformers **a** and **b** in ozonides **23—28** depends on the nature of a substituents in the aryl group, as well as on the presence of substituent at the atom C(10). From the relative intensity of two signals for the proton H(1) (see Table 2, the more high-field signal is assigned, according to the

Table 2. The ^1H and ^{13}C NMR spectra (δ, *J*/Hz) of ozonides **24—28** (conformers **a** and **b**)* and **29**

Group or atom**	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
	Compound **24a [24b]**		Compound **25a [25b]**		Compound **26a [26b]**	
C(1)H	99.08 [101.06]	6.37 (br.s) [6.47 (s)]	99.09 [101.10]	6.38 (br.s) [6.47 (s)]	99.02 [101.03]	6.37 (d, $J_{H(1),H(11b)}$ = 2.4); [6.50 (s)]
C(4)H	99.08 [101.06]	5.79 (d, $J_{H(4),H(5)}$ = 3.6) [5.61 (s)]	99.09 [101.06]	5.80 (d, $J_{H(4),H(5)}$ = 4) [5.61 (s)]	99.18 [101.03]	5.79 (d, $J_{H(4),H(5)}$ = 3.6) [5.60 (s)]
C(5)H_2	30.22	1.77 (m); 2.27 (m)	30.27	1.74 (m); 2.25 (m)	29.34	1.78 (m); 2.28 (m)
C(5a)H	32.83	3.29 (m)	31.24	3.28 (m)	29.68	3.34 (m)
C(6)H	58.14 (br.s) [58.86]	5.87 (d, $J_{H(6),H(5a)}$ = 11.2)	57.88 (br.s) [58.75]	5.89 (d, $J_{H(6),H(5a)}$ = 11.2)	58.06 (br.s) [59.00]	5.90 (d, $J_{H(6),H(5a)}$ = 10.8)
C(7a)	137.16	—	136.67	—	139.15	—
C(8)H—C(11)H	126.64, 127.65, 127.84, 127.97	6.18 (m)	126.51, 127.66, 127.93, 128.25	6.14 (m)	124.95, 125.20, 126.50, 126.67	7.38 (m)
C(11a)	130.09	—	133.67	—	131.45	—
C(11b)H	38.39 [39.06]	3.58 (dd, $J_{H(11b),H(5a)}$ = 10.8, $J_{H(11b),H(1)}$ = 3.4) [3.14 (m)]	38.40 [39.05]	3.57 (dd, $J_{H(11b),H(5a)}$ = 10.8, $J_{H(11b),H(1)}$ = 3.4) [3.12 (m)]	38.37 [39.09]	3.58 (dd, $J_{H(11b),H(5a)}$ = 10.8, $J_{H(11b),H(1)}$ = 2.4) [3.16 (m)]
C(1′)	135.62	—	135.57	—	135.57	—
C(2′)H	128.45	6.18 (m)	128.50	6.14 (m)	127.77	7.38 (m)
C(3′)H	—	—	128.83	6.14 (m)	128.01	7.38 (m)
C(3′)	133.81	—	—	—	—	—
C(4′)H	129.20	6.18 (m)	—	—	—	—
C(4′)	—	—	134.31	—	131.45	—
C(5′)H, C(6′)H	127.65, 126.64	6.18 (m)	129.10, 131.08	6.14 (m)	130.08, 130.19	7.38 (m)
C(4′)$\underline{C}F_3$	—	—	—	—	122.49 (q, $^1J_{CF}$ = 272)	—
CF_3CO	155.61 (q, C=O, $^2J_{CF}$ = 37); 116.52 (q, CF_3, $^1J_{CF}$ = 289)	—	155.55 (q, C=O, $^2J_{CF}$ = 36) [156.91 (q, C=O, $^1J_{CF}$ = 36)]; 116.51 (q, CF_3, $^1J_{CF}$ = 288)	—	156.00 (q, $^2J_{CF}$ = 36); 115.92 (q, $^1J_{CF}$ = 289)	—
10-CO_2Me	—	—	165.96 (C=O); 52.45 (Me—O)	3.96 (s, Me—O)	—	—
4-CO_2Et	—	—	—	—	167.60 (C=O); 61.78 (CH_2—O); 13.72 (Me)	4.14 (m, CH_2—O); 1.18 (m, Me)
	Compound **27a [27b]**		Compound **28a [28b]**		Compound **29**	
C(1)H	98.93 [101.15]	6.41 (br.s) [6.47 (s)]	98.87	6.44 (d, $J_{H(1),H(11b)}$ = 2.8) [6.54 (s)]	101.49	6.06 (s)
C(4)H	99.21 [101.31]	5.82 (d, $J_{H(4),H(5)}$ = 5.2) [5.60 (br.s)]	99.09	5.81 (d, $J_{H(4),H(5)}$ = 5.2) [5.62 (s)]	99.62	5.85 (s)

(*to be continued*)

Table 2 (*continued*)

Group or atom**	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
	Compound **27a** [**27b**]		Compound **28a** [**28b**]		Compound **29**	
$C(5)H_2$	30.51 [32.94]	1.77 (m); 2.28 (m)	30.24	1.84 (m); 2.28 (m)	28.96	2.39 (m); 2.57 (m)
C(5a)H	31.23	3.30 (m)	31.38	3.32 (m)	32.83	3.27 (m)
C(6)H	58.46 (br.s) [59.34 (s)]	5.90 (d, $J_{H(6),H(5a)} = 10.8$)	58.86 (br.s)	5.90 (d, $J_{H(6),H(5a)} = 10.8$)	58.08 (br.s)	4.91 (m)
C(7a)	137.75	—	140.06	—	136.22	—
C(8)H—C(11)H	126.33, 126.53, 127.36, 127.77	7.03 (m)	126.50, 127.89, 128.17, 131.33	7.09 (m)	126.78, 127.27	7.41 (m)
C(11a)	131.77	—	134.95	—	127.48	—
C(11b)H	38.72 [39.15]	3.58 (dd, $J_{H(11b),H(5a)} = 11.6$, $J_{H(11b),H(1)} = 3.2$)	38.49	3.60 (dd, $J_{H(11b),H(5a)} = 11.2$, $J_{H(11b),H(1)} = 2.4$)	38.04	3.48 (d, $J_{H(11b),H(5a)} = 8.4$)
C(1´)	134.97 [135.15]	—	138.42	—	—	—
C(2´)H	127.87	7.03 (m)	128.46	7.09 (m)	—	—
C(3´)H	128.46	7.03 (m)	128.78	7.09 (m)	—	—
C(3´)	133.81	—	—	—	—	—
C(4´)H	—	—	129.19	7.09 (m)	—	—
C(4´)	135.96	—	—	—	—	—
C(5´)H, C(6´)H	128.96, 129.90	7.03 (m)	129.90, 129.58	7.09 (m)	—	—
C(4´)Me	21.25 [21.45]	2.19 (s)	—	—	—	—
CF_3CO	155.47 (q, C=O, $^2J_{CF} = 36$); 116.61 (q, CF_3, $^1J_{CF} = 283$)	—	155.51 (q, C=O, $^2J_{CF} = 37$); 116.54 (q, CF_3, $^1J_{CF} = 289$)	—	156.53 (m, C=O); 116.40 (q, CF_3, $^1J_{CF} = 288$	—
10-CO_2Me	—	—	165.96 (C=O); 52.45 (Me—O)	3.96 (s, Me—O)	—	—
4-CO_2Et	—	—	—	—	167.60 (C=O); 61.78 (CH_2—O); 13.72 (Me)	4.14 (m, CH_2—O); 1.18 (m, Me)

* If signals for conformers **a** and **b** overlap, only one δ_C and δ_H value is given.
** The atoms C(1´)—C(6´) are from the aryl group.

literature data,[20] to the major conformer **a**) or H(4) (the signal for the major conformer **a** is found more downfield) it follows that the ratio of conformers **a** and **b** in ozonides **23—28** is ~70 : 30 (**23**),[20] 92 : 8 (**24**), 88 : 12 (**25** and **26**), 89 : 11 (**27**), 99 : 1 (**28**). Due to the pseudoaxial position of the trifluoroacetyl group intrinsic to conformers **b**, this group is close to the trioxolane ring, that makes the conformational transformations difficult to occur because of the donor-acceptor interaction of p-electrons of the O atoms of the trioxolane ring with strongly electronegative F atoms of the trifluoromethyl group.[20] A narrow signal for the atom C(6) (δ 58.8—59.3) neighboring to the N atom indicates degree of rigidity of conformers **b**, whereas this signal is broadened in the spectra of conformers **a**, that shows the presence of the exchange process between energetically close conformers.

In ozonides **23—29**, the protons at the chiral vicinal atoms C(5a), C(6), and C(11b) are *cis*-oriented with

respect to each other, which is indicated by their spin-spin coupling constant values ($J_{H(6),H(5a)} \approx 11$ Hz, $J_{H(11b),H(5a)} = 8.4$—11.6 Hz) (see Table 2). Based on the ^1H and ^{13}C NMR spectra and the X-ray diffraction data obtained earlier[20] for *N*-acetoxy ozonide related to compound **23**, the structure of (1*R**,4*S**,5a*R**,6*S**,11b*R**)-6-aryl-7-trifluoroacetyl-4,5,5a,6,7,11b-hexahydro-1*H*-1,4-epoxy[1,2]dioxepino[5,4-*c*]quinoline is assigned to ozonides **24—28** (a methoxycarbonyl group at the atom C(10) is additionally present in compound **28**, whereas compound **29** has a CO_2Et group instead of the aryl group at position C(6)).

In conclusion, a three-component condensation of arylammonium trifluoroacetate, an aldehyde, and cyclopentadiene in MeCN with subsequent *N*-trifluoroacetylation and ozonolysis furnishes new stable ozonides — promising antimalaria peroxide-type agents.

Experimental

^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 (400.13 (^1H) and 100.62 (^{13}C) MHz) spectrometer in $CDCl_3$ using Me_4Si as an internal standard. The homo- and heteronuclear procedures DEPT-135°, COSY, HSQC, HMBC corresponded to the standard Bruker procedures. Melting points were measured on a small-size Boetius heating stage. Elemental analysis was performed on a Carlo Erba EA-1108 CHNS-O-analyser. Silica gel KSKG (100/200) was used for column chromatography. Plates with SiO_2 (Silufol) were used for the monitoring by TLC, a solution of vanillin in ethanol acidified with sulfuric acid was used for visualization.

The starting compounds **1—7** were purchased from Acros Organics, compound **8** from Fluka. The ^1H and ^{13}C NMR spectra of compounds **17—22** are given in Table 1, of compounds **24—29** in Table 2, the NMR spectra of compounds **16** and **23** have been reported earlier.[20]

(3a*R,4*S**,9b*S**)-4-(3-Chlorophenyl)-5-trifluoroacetyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline (17).** Trifluoroacetic acid (TFA) (0.23 mL, 3 mmol) was added to a solution of aniline (**1**) (0.27 mL, 3.0 mmol) in anhydrous MeCN (30 mL), followed by addition of freshly distilled cyclopentadiene (CPD) (1.23 mL, 15 mmol) at 0 °C and 3-chlorobenzaldehyde (**4**) (0.34 mL, 3 mmol). The reaction mixture was stirred at ~20 °C until the starting aniline disappeared (0.25 h, TLC monitoring, *n*-hexane—ethyl acetate, 3 : 1). The solvent was evaporated, the residue was diluted with saturated aqueous $NaHCO_3$ until neutrality (~6 mL) and extracted with ethyl acetate. The organic layer was concentrated, the residue was subjected to column chromatography (a column 20 mm in diameter, 5—10 g of SiO_2, *n*-hexane was an eluent). The yield of compound **10** was 0.83 g (98%), R_f 0.70 (*n*-hexane—ethyl acetate, 3 : 1), m.p. 118—120 °C (from *n*-hexane). Found (%): C, 76.68; H, 5.60; Cl, 12.82; N, 4.73. $C_{18}H_{16}ClN$. Calculated (%): C, 76.72; H, 5.72; Cl, 12.58; N, 4.97. ^1H NMR ($CDCl_3$), δ: 1.88 (dd, 1 H, $H_a(3)$, J = 8.4 Hz, J = 16.0 Hz); 2.67 (m, 1 H, $H_e(3)$); 3.05 (q, 1 H, H(3a), J = 8.8 Hz); 3.75 (br.s, 1 H, H(5)); 4.17 (d, 1 H, H(9b), J = 8.8 Hz); 4.66 (d, 1 H, H(4), J = 2.8 Hz); 5.72 (s, 1 H, H(2)); 5.92 (s, 1 H, H(1)); 6.69 (d, 1 H, H(9), J = 7.6 Hz); 6.84 (t, 1 H, H(7), J = 7.6 Hz); 7.07 (t, 1 H, H(8), J = 7.6 Hz); 7.13 (d, 1 H, H(6), J = 7.6 Hz); 7.35 (br.s, 1 H, $H_{Ar}(6')$); 7.36 (br.s, 1 H, $H_{Ar}(5')$); 7.38 (br.s, 1 H, $H_{Ar}(4')$); 7.52 (br.s, 1 H, $H_{Ar}(2')$). ^{13}C NMR ($CDCl_3$), δ: 31.48 (C(3)); 45.91 (C(3a)); 46.31 (C(9b)); 57.66 (C(4)); 116.12 (C(9)); 119.51 (C(7)); 124.77 (C(4′)); 126.01 (C(9a)); 126.47 (C(8)); 126.69 (C(5′)); 127.48 (C(6′); 129.07 (C(6)); 129.86 (C(2′)); 130.31 (C(2)); 134.04 (C(1)); 134.50 (C(3′)); 145.11(C(1′)); 145.22 (C(5a)). Trifluoroacetic anhydride (TFAA) (0.34 mL, 2.4 mmol) and triethylamine (0.33 mL, 2.4 mmol) were added to a solution of compound **10** (0.56 g, 2.0 mmol) in anhydrous CH_2Cl_2 (10 mL). The reaction mixture was stirred until the starting compound disappeared (2 min, TLC monitoring, *n*-hexane—ethyl acetate, 3 : 1). The solvent was evaporated, the residue was diluted with saturated aq. $NaHCO_3$ until neutrality (~5 mL) and extracted with ethyl acetate. The organic layer was concentrated, the residue was subjected to column chromatography (a column 20 mm in diameter, 5—10 g of SiO_2, light petroleum (b.p. 70—100 °C) was an eluent). The yield of trifluoroacetamide **17** was 0.73 g (97%), R_f 0.61 (*n*-hexane—ethyl acetate, 3 : 1), m.p. 50—52 °C. Found (%): C, 63.73; H, 3.85; Cl, 9.62; N, 3.74. $C_{20}H_{15}ClF_3NO$. Calculated (%): C, 63.58; H, 4.00; Cl, 9.38; N, 3.71.

(3a*R,4*S**,9b*S**)-4-(4-Chlorophenyl)-5-trifluoroacetyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline (18).** Trifluoroacetic acid (0.23 mL, 3.0 mmol) was added to a solution of aniline (**1**) (0.27 mL, 3.0 mmol) in anhydrous acetonitrile (20 mL), followed by addition of freshly distilled CPD (1.23 mL, 15 mmol) at 0 °C and 4-chlorobenzaldehyde (**5**) (0.34 mL, 3.0 mmol). The mixture was stirred for 0.5 h and further treated as described in the synthesis of compound **10**. The yield of compound **11** was 0.76 g (90%), R_f 0.58 (*n*-hexane—ethyl acetate, 3 : 1), m.p. 138—140 °C (from *n*-hexane) (the data in Ref. 26: m.p. 141—142 °C). ^1H NMR ($CDCl_3$), δ (*cf.* Ref. 26): 1.86 (dd, 1 H, $H_a(3)$, J = 8.8 Hz, J = 16.4 Hz); 2.65 (m, 1 H, $H_e(3)$); 3.02 (q, 1 H, H(3a), J = 9.2 Hz); 3.73 (br.s, 1 H, H(5)); 4.17 (d, 1 H, H(9b), J = 8.8 Hz); 4.66 (d, 1 H, H(4), J = 2.8 Hz); 5.71 (s, 1 H, H(2)); 5.92 (s, 1 H, H(1)); 6.68 (d, 1 H, H(9), J = 7.6 Hz); 6.83 (t, 1 H, H(7), J = 7.6 Hz); 7.06 (t, 1 H, H(8), J = 7.6 Hz); 7.12 (d, 1 H, H(6), J = 7.6 Hz); 7.39 (d, 2 H, $H_{Ar}(2')$, $H_{Ar}(6')$, J = 8.0 Hz); 7.42 (d, 2 H, $H_{Ar}(3')$, $H_{Ar}(5')$, J = 8.0 Hz). ^{13}C NMR ($CDCl_3$), δ (*cf.* Ref. 26): 31.45 (C(3)); 45.97 (C(3a)); 46.31 (C(9b)); 57.53 (C(4)); 116.07 (C(9)); 119.46 (C(7)); 126.02 (C(9a)); 126.45 (C(8)); 127.90 (C(3′), C(5′)); 128.71 (C(2′), C(6′)); 129.07 (C(6)); 130.30 (C(2)); 132.91 (C(4′)); 134.07 (C(1)); 141.43 (C(1′)); 145.32 (C(5a)). Compound **11** (0.56 g, 2.0 mmol), TFAA (0.34 mL, 2.4 mmol), and Et_3N (0.33 mL, 2.4 mmol) under conditions for the synthesis of trifluoroacetate **17** furnished amorphous trifluoroacetamide **18** (34 g, 90%), R_f 0.53 (*n*-hexane—ethyl acetate, 3 : 1). Found (%): C, 63.57; H, 3.79; Cl, 9.43; N, 3.62. $C_{20}H_{15}ClF_3NO$. Calculated (%): C, 63.58; H, 4.00; Cl, 9.38; N, 3.71.

(3a*R,4*S**,9b*S**)-5-Trifluoroacetyl-4-(4-trifluoromethylphenyl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline (19).** Trifluoroacetic acid (0.31 mL, 4.0 mmol) was added to a solution of aniline (**1**) (0.36 mL, 4.0 mmol) in anhydrous MeCN (15 mL), followed by addition of freshly distilled CPD (1.64 mL, 20 mmol) at 0 °C and 4-trifluoromethylbenzaldehyde (**6**) (0.55 g, 4 mmol). The mixture was stirred for 1 h and further treated as described in the synthesis of compound **10**. The yield of compound **12** was 1.08 g (86%), R_f 0.67 (*n*-hexane—ethyl acetate, 3 : 1), m.p. 108—110 °C. Found (%): C, 72.42; H, 5.00; N, 4.50. $C_{19}H_{16}F_3N$. Calculated (%): C, 72.37; H, 5.11; N, 4.44). ^1H NMR ($CDCl_3$),

δ: 1.85 (dd, 1 H, H_a(3), J = 8.8 Hz, J = 16.4 Hz); 2.68 (m, 1 H, H_e(3)); 3.08 (q, 1 H, H(3a), J = 8.8 Hz); 3.78 (br.s, 1 H, H(5)); 4.21 (d, 1 H, H(9b), J = 8.8 Hz); 4.76 (d, 1 H, H(4), J = 2.4 Hz); 5.72 (s, 1 H, H(2)); 5.94 (s, 1 H, H(1)); 6.71 (d, 1 H, H(9), J = 8.0 Hz); 6.86 (t, 1 H, H(7), J = 8.0 Hz); 7.08 (t, 1 H, H(8), J = 8.0 Hz); 7.15 (d, 1 H, H(6), J = 8.0 Hz); 7.63 (d, 2 H, H_{Ar}(2′), H_{Ar}(6′), J = 8.4 Hz); 7.71 (d, 2 H, H_{Ar}(3′), H_{Ar}(5′), J = 8.4 Hz). ^{13}C NMR ($CDCl_3$), δ: 31.43 (C(3)); 45.87 (C(9b)); 46.32 (C(3a)); 57.84 (C(4)); 113.89 (CF_3, J = 280.5 Hz); 116.15 (C(9)); 119.63 (C(7)); 125.50 (C(6′)); 125.54 (C(9a)); 126.01 (C(2′)); 126.51 (C(8)); 126.89 (C(6), C(3′), C(5′)); 129.09 (C(2)); 130.22 (C(1)); 134.04 (C(4′)); 145.12 (C(1′)); 147.00 (C(5a)). Compound **12** (0.63 g, 2.0 mmol), TFAA (0.34 mL, 2.4 mmol), and Et_3N (0.33 mL, 2.4 mmol) under conditions for the synthesis of compound **17** furnished amorphous trifluoroacetamide **19** (0.72 g, 88%), R_f 0.62 (*n*-hexane—ethyl acetate, 3 : 1). Found (%): C, 61.41; H, 3.57; N, 3.62. $C_{21}H_{15}F_6NO$. Calculated (%): C, 61.32; H, 3.68; N, 3.41.

(3a*R,4*S**,9b*S**)-4-(4-Methylphenyl)-5-trifluoroacetyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline (20).** Freshly distilled CPD (2.05 mL, 25 mmol) was added to a solution of aniline (**1**) (0.46 mL, 5.0 mmol) and TFA (0.39 mL, 5.0 mmol) in anhydrous MeCN (50 mL) at 0 °C, followed by addition of 4-methylbenzaldehyde (**7**) (0.59 mL, 5.0 mmol), the mixture was stirred for 3 h and further treated as described for the synthesis of compound **10**. The yield of compound **13** was 0.78 g (60%), R_f 0.56 (*n*-hexane—ethyl acetate, 3 : 1), m.p. 100—102 °C (from *n*-hexane) (the data in Ref. 26: m.p. 64—65 °C). ^{1}H NMR ($CDCl_3$), δ (*cf.* Ref. 26): 1.97 (dd, 1 H, H_a(3), J = 8.8 Hz, J = 16.0 Hz); 2.52 (s, 3 H, MeC(4′)); 2.79 (m, 1 H, H_e(3)); 3.14 (q, 1 H, H(3a), J = 8.8 Hz); 3.83 (m, 1 H, H(5)); 4.24 (d, 1 H, H(9b), J = 8.0 Hz); 4.72 (br.s, 1 H, H(4)); 5.79 (s, 1 H, H(2)); 5.98 (s, 1 H, H(1)); 6.71 (d, 1 H, H(9), J = 8.0 Hz); 6.86 (t, 1 H, H(7), J = 8.0 Hz); 7.08 (t, 1 H, H(8), J = 8.0 Hz); 7.15 (d, 1 H, H(6), J = 8.0 Hz); 7.63 (d, 2 H, H_{Ar}(2′), H_{Ar}(6′), J = 8.4 Hz); 7.71 (d, 2 H, H_{Ar}(3′), H_{Ar}(5′), J = 8.4 Hz). ^{13}C NMR ($CDCl_3$), δ (*cf.* Ref. 26): 21.71 (Me); 31.67 (C(3)); 43.22 (C(3a)); 46.16 (C(9b)); 58.18 (C(4)); 116.06 (C(9)); 119.26 (C(7)); 123.67 (C(5′)); 126.25 (C(6)); 126.44 (C(6′)); 126.60 (C(8)); 127.34 (C(9a)); 128.22 C(3′)); 128.67 (C(2′)); 130.51 (C(2)); 132.16 (C(1)); 142.96 (C(4′)); 145.83 (C(1′)); 148.37 (C(5a)). Compound **13** (0.52 g, 2.0 mmol), TFAA (0.34 mL, 2.4 mmol), and Et_3N (0.33 mL, 2.4 mmol) under conditions for the synthesis of trifluoroacetamide **17** furnished amorphous product **20** (0.64 g, 90%), R_f 0.50 (*n*-hexane—ethyl acetate, 3 : 1). Found (%): C, 70.57; H, 4.96; N, 3.89. $C_{21}H_{18}F_3NO$. Calculated (%): C, 70.58; H, 5.08; N, 3.92.

(3a*R,4*S**,9b*S**)-8-Methoxycarbonyl-4-phenyl-5-trifluoroacetyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline (21).** The reaction of methyl 4-aminobenzoate (**7**) (0.75 g, 5.0 mmol), TFA (0.39 mL, 5.0 mmol), freshly distilled CPD (2.05 mL, 25 mmol), and benzaldehyde (**3**) (0.51 mL, 5 mmol) under conditions for the synthesis of compound **10** yielded compound **14** (1.2 g, 78%), R_f 0.60 (*n*-hexane—ethyl acetate, 3 : 1), m.p. 127—129 °C. Found (%): C, 78.63; H, 6.20; N, 4.52. $C_{20}H_{19}NO_2$. Calculated (%): C, 78.66; H, 6.27; N, 4.59. ^{1}H NMR ($CDCl_3$), δ: 1.83 (m, 1 H, H_a(3)); 2.60 (m, 1 H, H_e(3)); 3.03 (q, 1 H, H (3a), J = 8.8 Hz); 3.87 (s, MeO); 4.14 (d, 1 H, H(9b), J = 8.4 Hz); 4.71 (d, 1 H, H(4), J = 2.4 Hz); 5.68 (s, 1 H, H(2)); 5.93 (s, 1 H, H(1)); 6.61 (d, 1 H, H(6), J = 8.0 Hz); 7.33 (m, 6 H, H(7), H_{Ar}(2′), H_{Ar}(3′), H_{Ar}(4′), H_{Ar}(6′), H_{Ar}(5′)); 7.84 (s, 1 H, H(9)). ^{13}C NMR ($CDCl_3$), δ: 31.52 (C(3)); 45.78 (C(3a)); 45.89 (C(9b)); 51.63 (MeO); 57.52 (C(4)); 115.13 (C(6)); 120.23 (C(8)); 125.07 (C(9a)); 126.40 C(3′), C(5′)); 127.53 (C(7)); 128.41 (C(4′)); 128.64 (C(2′), C(6′)); 130.49 (C(2)); 131.19 (C(9)); 133.91 (C(1)); 142.03 (C(1′)); 149.95 (C(5a)); 167.63 (C=O). Compound **14** (0.61 g, 2.0 mmol), TFAA (0.34 mL, 2.4 mmol), and Et_3N (0.33 mL, 2.4 mmol) under conditions for the synthesis of trifluoroacetamide **17** furnished product **21** (0.72 g, 90%), R_f 0.50 (*n*-hexane—ethyl acetate, 3 : 1), m.p. 61—63 °C. Found (%): C, 65.80; H, 4.40; N, 3.62. $C_{22}H_{18}F_3NO_3$. Calculated (%): C, 65.83; H, 4.52; N, 3.49.

(3a*R,4*S**,9b*S**)-4-Ethoxycarbonyl-5-trifluoroacetyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline (22).** Trifluoroacetic acid (0.77 mL, 10 mmol) was added to a solution of aniline (**1**) (0.91 mL, 10 mmol) in anhydrous MeCN (60 mL), followed by addition of freshly distilled CPD (4.1 mL, 50 mmol) at 0 °C and ethyl glyoxylate (**8**) (50% solution in toluene) (2 mL, 10 mmol). After the reaction was performed, the mixture was treated as described for the synthesis of compound **10**. The yield of compound **15** was 1.36 g (56%), R_f 0.63 (*n*-hexane—ethyl acetate, 3 : 1), m.p. 60—62 °C (from *n*-hexane). Found (%): C, 74.00; H, 6.78; N, 5.96. $C_{15}H_{17}NO_2$. Calculated (%): C, 74.05; H, 7.04; N, 5.76. ^{1}H NMR ($CDCl_3$), δ: 1.37 (m, Me); 2.38 (m, 1 H, H(3)); 2.54 (m, 1 H, H(3)); 3.39 (q, 1 H, H(3a), J = 8.8 Hz); 4.12 (br.s, 1 H, H(5)); 4.13 (m, CH_2O); 4.25 (d, 1 H, H(9b), J = 8.0 Hz); 4.35 (d, 1 H, H(4), J = 7.2 Hz); 5.71 (s, 1 H, H(2)); 5.78 (s, 1 H, H(1)); 6.68 (d, 1 H, H(9), J = 7.6 Hz); 6.77 (t, 1 H, H(7), J = 7.6 Hz); 7.01 (t, 1 H, H(8), J = 7.6 Hz); 7.05 (d, 1 H, H(6), J = 7.6 Hz). ^{13}C NMR ($CDCl_3$), δ: 14.32 (MeCH$_2$O); 32.70 (C(3)); 40.82 (C(3a); 46.45 (C(9b)); 56.51 (C(4)); 61.22 (CH_2O); 115.79 (C(6)); 119.25 (C(7)); 125.98 (C(9a)); 126.50 (C(9)); 128.67 (C(8)); 129.82 (C(1)); 134.28 (C(2)); 144.00 (C(5a)); 171.95 (C=O). Compound **15** (1.22 g, 5.0 mmol), TFAA (0.85 mL, 5 mmol), Et_3N (0.69 mL, 5 mmol), and anhydrous CH_2Cl_2 (30 mL) under conditions for the synthesis of trifluoroacetamide **17** furnished product **22** (1.02 g, 60%), R_f 0.64 (*n*-hexane—ethyl acetate, 3 : 1), m.p. 86—88 °C. Found (%): C, 60.45; H, 4.67; N, 4.38. $C_{17}H_{16}F_3NO_3$. Calculated (%): C, 60.18; H, 4.75; N, 4.13.

(1*R,4*S**,5a*R**,6*S**,11b*R**)-6-(3-Chlorophenyl)-7-trifluoroacetyl-4,5,5a,6,7,11b-hexahydro-1*H*-1,4-epoxy[1,2]dioxepino-[5,4-*c*]quinoline (24).** The ozone-oxygen mixture (the ozonator productivity was (30 mmol of O_3) h^{-1}) was passed through a solution of compound **17** (0.57 g, 1.5 mmol) in anhydrous CH_2Cl_2 (20 mL) at 0 °C with stirring until the starting compound disappeared (~3 min, TLC monitoring). The reaction mixture was purged with argon and concentrated. The residue was subjected to column chromatography (10 g of SiO_2 with $CHCl_3$ as an eluent). The yield of ozonide **24** was 0.47 g (73%), R_f 0.28 ($CHCl_3$), m.p. 48—50 °C, the ratio of conformers **24a** : **24b** = 92 : 8 (from relative intensities of signals for the atom H(1) (δ 6.37 and 6.47) or H(4) (δ 5.79 and 5.61)). Found (%): C, 56.60; H, 3.41; Cl, 8.42; N, 3.20. $C_{20}H_{15}ClF_3NO_4$. Calculated (%): C, 56.42; H, 3.55; Cl, 8.33; N, 3.29.

(1*R,4*S**,5a*R**,6*S**,11b*R**)-6-(4-Chlorophenyl)-7-trifluoroacetyl-4,5,5a,6,7,11b-hexahydro-1*H*-1,4-epoxy[1,2]dioxepino-[5,4-*c*]quinoline (25).** Ozonation of compound **18** (0.57 g, 1.5 mmol) and subsequent treatment as described in the preceding experiment yielded ozonide **25** (0.22 g, 34%), R_f 0.27 ($CHCl_3$), m.p. 58—60 °C, the ratio of conformers **25a** : **25b** = 88 : 12 (from relative intensities of signals for the atom H(1) (δ 6.38 and 6.47) or

H(4) (δ 5.80 and 5.61)). Found (%): C, 56.42; H, 3.42; Cl, 8.12; N, 3.50. $C_{20}H_{15}ClF_3NO_4$. Calculated (%): C, 56.42; H, 3.55; Cl, 8.33; N, 3.29.

(1*R,4*S**,5a*R**,6*S**,11b*R**)-7-Trifluoroacetyl-6-(4-trifluoromethylphenyl)-4,5,5a,6,7,11b-hexahydro-1*H*-1,4-epoxy[1,2]-dioxepino[5,4-*c*]quinoline (26).** The reaction of compound **19** (0.62 g, 1.5 mmol) as described in the synthesis of ozonide **24** gave ozonide **26** (0.49 g, 71%), R_f 0.50 ($CHCl_3$), m.p. 36—38 °C, the ratio of conformers **26a** : **26b** = 88 : 12 (from relative intensities of signals for the atom H(1) (δ 6.37 and 6.50) or H(4) (δ 5.79 and 5.60)). Found (%): C, 54.92; H, 3.18; N, 3.18. $C_{21}H_{15}F_6NO_4$. Calculated (%): C, 54.91; H, 3.29; N, 3.05.

(1*R,4*S**,5a*R**,6*S**,11b*R**)-6-(4-Methylphenyl)-7-trifluoroacetyl-4,5,5a,6,7,11b-hexahydro-1*H*-1,4-epoxy[1,2]dioxepino[5,4-*c*]quinoline (27).** The reaction of compound **20** (0.54 g, 1.5 mmol) as described in the synthesis of ozonide **24** gave ozonide **27** (0.21 g, 34%), R_f 0.38 ($CHCl_3$), m.p. 50—52 °C, the ratio of conformers **27a** : **27b** = 89 : 11 (from relative intensities of signals for the atom H(1) (δ 6.41 and 6.47) or H(4) (δ 5.82 and 5.60)). Found (%): C, 62.31; H, 4.37; N, 3.87. $C_{21}H_{18}F_3NO_4$. Calculated (%): C, 62.22; H, 4.48; N, 3.46.

(1*R,4*S**,5a*R**,6*S**,11b*R**)-10-Methoxycarbonyl-6-phenyl-7-trifluoroacetyl-4,5,5a,6,7,11b-hexahydro-1*H*-1,4-epoxy[1,2]-dioxepino[5,4-*c*]quinoline (28).** The reaction of compound **21** (0.60 g, 1.5 mmol) as described in the synthesis of ozonide **24** gave ozonide **28** (0.08 g, 18%), R_f 0.23 ($CHCl_3$), m.p. 62—64 °C, the ratio of conformers **28a** : **28b** = 99 : 1 (from relative intensities of signals for the atom H(1) (δ 6.44 and 6.54) or H(4) (δ 5.81 and 5.62)). Found (%): C, 59.25; H, 4.01; N, 3.02. $C_{22}H_{18}F_3NO_6$. Calculated (%): C, 58.80; H, 4.04; N, 3.12.

(1*R,4*S**,5a*R**,6*S**,11b*R**)-6-Ethoxycarbonyl-7-trifluoroacetyl-4,5,5a,6,7,11b-hexahydro-1*H*-1,4-epoxy[1,2]dioxepino-[5,4-*c*]quinoline (29).** The reaction of compound **22** (1.02 g, 3.0 mmol) as described in the synthesis of ozonide **24** gave ozonide **29** (0.14 g, 12%), R_f 0.19 ($CHCl_3$), m.p. 48—50 °C. Found (%): C, 52.80; H, 4.12; N, 3.58. $C_{17}H_{16}F_3NO_6$. Calculated (%): C, 52.72; H, 4.16; N, 3.62.

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