# Synthesis of 4-Aryl-8-fluoro-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolines and Their Ozonides

by **Alexander G. Tolstikov**, **Rimma G. Savchenko***, **Elena S. Lukina**, **Denis V. Nedopekin**, **Regina M. Limantceva**, **Leonard M. Khalilov**, **Ekaterina S. Mescheryakova**, and **Victor N. Odinokov**

Institute of Petrochemistry and Catalysis, Russian Academy of Sciences, pr. Oktyabrya, 141, RU-450075 Ufa (fax: +73472842750; e-mail: rimasavchenko@mail.ru)

4-Aryl-8-fluoro-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolines are synthesized by acid-catalyzed ($CF_3CO_2H$) three-component cyclocondensation of 4-fluoroaniline with aromatic aldehydes and cyclopentadiene. Stable ozonides with (1*R**,4*S**,5a*R**,6*S**,11b*S**)-configurations are obtained by ozonolysis of corresponding trifluoroacetyl derivatives.

**Introduction.** – The tetrahydroquinoline skeleton is often used for the design of many synthetic compounds with diverse pharmacological properties. The fluorinated heterocyclic compounds possess a broad spectrum of biological activities [1][2]. A special interest is focused on derivatives of 6-fluoroquinolines. Due to interesting chemical or biological properties of F-bearing tetrahydroquinolines, the synthesis of this class of azaheterocyclic compounds has attracted broad interest [3–5].

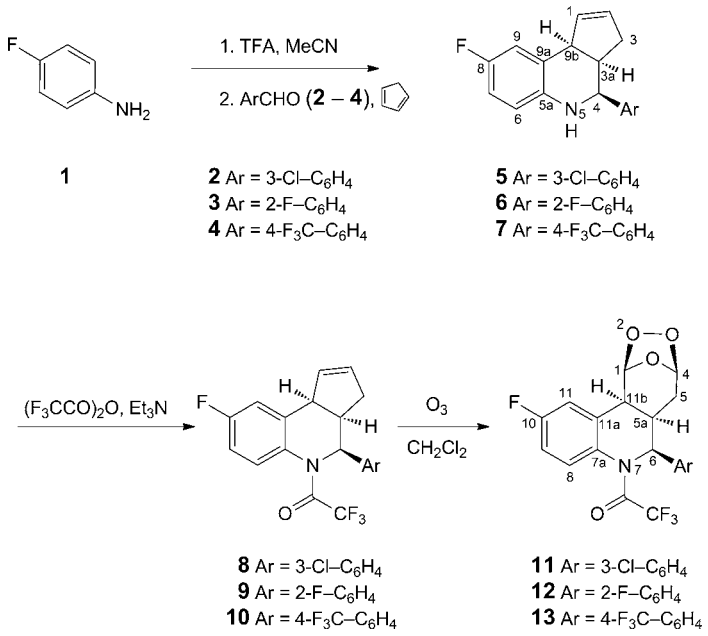
The aza-*Diels–Alder* reaction (*Povarov* reaction; cyclocondensation of aromatic *Schiff* bases (anils) with electron-rich olefins) provides great opportunities in the formation of the quinoline skeleton [6][7]. One-step three-component reaction of substituted anilines with aldehydes and cyclopentadiene as a dienophile is one of the synthetically most attractive approachs [8]. This method opens a simple route to the synthesis of substituted tetrahydroquinolines [9].

Ozonolytic cleavage of the cycloalkenyl C=C bond in tetrahydroquinoline fused with cyclopentene affords the ozonides of aza-heterocycles [10]. To improve antimalaria or antiviral activity of synthetic peroxides and ozonides, their conjugates containing weakly basic functional groups and heterocycles were obtained [11].

Within this context, we report here a one-pot three-component cyclocondensation of 4-fluoroaniline with aromatic aldehydes and cyclopentadiene to synthesize 6-fluorotetrahydroquinoline annulated with cyclopentene for the following possibility to obtain their stable ozonides.

**Result and Discussion.** – The condensation of *in situ* generated trifluoroacetate of 4-fluorophenylammonium (prepared by mixing equimolar amounts of amine **1** and 2,2,2-trifluoroacetic acid (TFA)) with an equimolar amount of an aromatic aldehyde (3-chloro-, 2-fluoro-, and 4-(trifluoromethyl)benzaldehyde (**2**–**4**, resp.)) and the fivefold excess of cyclopentadiene under normal conditions occurs rapidly and quantitatively (*Scheme*; *cf.* [8][9]).

*Scheme*




**1**

**2** Ar = 3-Cl–$C_6H_4$
**3** Ar = 2-F–$C_6H_4$
**4** Ar = 4-$F_3C$–$C_6H_4$

**5** Ar = 3-Cl–$C_6H_4$
**6** Ar = 2-F–$C_6H_4$
**7** Ar = 4-$F_3C$–$C_6H_4$

**8** Ar = 3-Cl–$C_6H_4$
**9** Ar = 2-F–$C_6H_4$
**10** Ar = 4-$F_3C$–$C_6H_4$

**11** Ar = 3-Cl–$C_6H_4$
**12** Ar = 2-F–$C_6H_4$
**13** Ar = 4-$F_3C$–$C_6H_4$

The H-atoms at the stereogenic centers C(3a), C(4), and C(9b) in the cycloadducts **5**–**7** are *cis*-oriented relative to each other, as deduced from their spin-spin coupling-constant values ($J$ (3a,9b) = 8.8 and $J$ (4,3a) = 3.2–3.6 Hz; *Table 1*). The structure of the compound **5** was clearly confirmed by X-ray diffraction (*Fig. 1*) and shows a pseudo-equatorial position of the 4-Ar group. Since the spectra of the synthesized compounds **5**–**7** have convergence and similarity of the main signals, we consider that

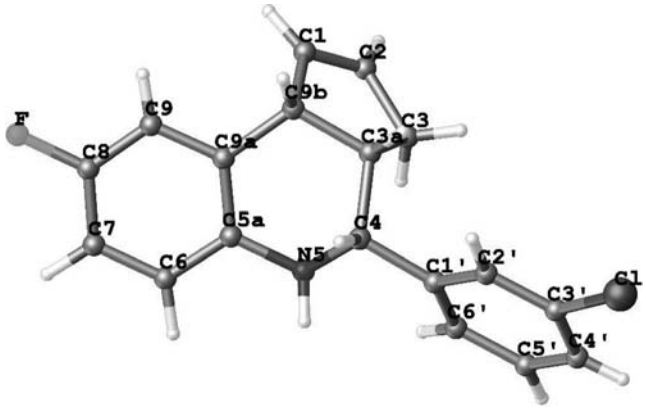



Fig. 1. *The molecular structure of (3a*R*,4*S*,9b*S*)-4-(3-chlorophenyl)-8-fluoro-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline* (**5**) *in the crystal*

Table 1. *The $^{1}H$- and $^{13}C$-NMR Data* ($\delta$ in ppm, $J$ in Hz) *of Compounds* **5**–**7**

| Position | Compound **5** | | Compound **6** | | Compound **7** | |
|---|---|---|---|---|---|---|
| | $\delta$(H) | $\delta$(C) | $\delta$(H) | $\delta$(C) | $\delta$(H) | $\delta$(C) |
| 1 | 5.88 (br. *s*) | 133.5 | 5.86 (br. *s*) | 133.6 | 5.85 (br. *s*) | 133.3 |
| 2 | 5.74 (br. *s*) | 130.9 | 5.77 (br. *s*) | 130.8 | 5.71 (br. *s*) | 130.8 |
| 3 | 1.88 (*dd*, $J$ = 16.0, 8.8), 2.66 (*ddd*, $J$ = 16.0, 9.2, 2.0) | 31.5 | 1.92 (*dd*, $J$ = 16.0, 9.4), 2.71 (*ddd*, $J$ = 16.0, 9.2, 2.0) | 31.8 | 1.82 (*dd*, $J$ = 16.0, 8.8), 2.62 (*ddd*, $J$ = 16.0, 9.2, 2.4) | 31.3 |
| 3a | 3.03 (*dd*, $J$ = 8.8, 3.2) | 45.6 | 3.25 (*dd*, $J$ = 8.8, 3.2) | 43.1 | 3.03 (*dd*, $J$ = 8.8, 3.2) | 45.4 |
| 4 | 4.59 (*d*, $J$ = 3.2) | 57.9 | 5.00 (br. *s*) | 51.4 | 4.68 (*d*, $J$ = 3.2) | 58.1 |
| 5a | – | 141.4 | – | 141.7 | – | 141.1 |
| 6 | 6.60–6.62 (*m*) | 115.8 (*d*, $^{3}J$(C,F) = 15.0) | 6.62 (*dd*, $^{3}J$(H,H) = 8.8, $^{4}J$(H,F) = 4.8) | 115.3 (*d*, $^{3}J$(C,F) = 16.0) | 6.62 (*dd*, $^{3}J$(H,H) = 8.8, $^{4}J$(H,F) = 4.8) | 116.8 (*d*, $^{3}J$(C,F) = 7.0) |
| 7 | 6.79 (*ddd*, $J$(H,H) = 8.4, 2.6, $^{3}J$(H,F) = 8.4) | 115.1 (*d*, $^{2}J$(C,F) = 22) | 6.85 (*ddd*, $J$(H,H) = 8.4, 2.8, $^{3}J$(H,F) = 8.4) | 115.1 (*d*, $^{2}J$(C,F) = 18.0) | 6.75 (*ddd*, $J$(H,H) = 8.4, 2.8, $^{3}J$(H,F) = 8.4) | 115.0 (*d*, $^{2}J$(C,F) = 22) |
| 8 | – | 156.7 (*d*, $^{1}J$(C,F) = 235.0) | – | 156.8(*d*, $^{1}J$(C,F) = 235.0) | – | 156.7 (*d*, $^{1}J$(C,F) = 236.0) |
| 9 | 6.86 (*dd*, $J$(H,H) = 2.4, $^{3}J$(H,F) = 9.2) | 113.2 (*d*, $^{2}J$(C,F) = 22.0) | 6.89 (*dd*, $J$(H,H) = 2.6, $J$(H,F) = 9.4) | 113.1 (*d*, $^{2}J$(C,F) = 23.0) | 6.82 (*dd*, $J$(H,H) = 2.8, $J$(H,F) = 9.2) | 113.6 (*d*, $^{3}J$(C,F) = 22.0) |
| 9a | – | 125.5 | – | 129.9 (*d*, $^{3}J$(C,F) = 12.0) | – | 125.5 |
| 9b | 4.13 (*d*, $^{3}J$(9b,3a) = 8.8) | 46.6 | 4.17 (*d*, $^{3}J$(9b,3a) = 8.8) | 46.5 | 4.13 (*d*, $^{3}J$(9b,3a) = 8.8) | 46.6 |
| 1′ | – | 144.9 | – | 124.3 (*d*, $^{2}J$(C,F) = 3.0) | – | 146.7 |
| 2′ | 7.52 (*s*) | 130.0 | – | 160.2 (*d*, $^{1}J$(C,F) = 245.0) | 7.59 (*d*, $J$ = 8.0) | 126.9 |
| 3′ | – | 134.6 | 7.11–7.19 (*m*) | 116.9 (*d*, $^{2}J$(C,F) = 4.0) | 7.67 (*d*, $^{3}J$(H,H) = 8.0) | 125.5 |
| 4′ | 7.42 (br. *s*) | 126.8 | 7.26–7.29 (*m*) | 127.7 (*d*, $^{3}J$(C,F) = 6.0) | – | 128.5 |
| 5′ | 7.36–7.38 (*m*) | 124.8 | 7.34–7.40 (*m*) | 127.3 (*d*, $^{4}J$(C,F) = 4.0) | 7.67 (*d*, $J$ = 8.0) | 125.5 |
| 6′ | 7.36–7.38 (*m*) | 127.5 | 7.68–7.72 (*m*) | 128.9 (*d*, $^{3}J$(C,F) = 11.0) | 7.59 (*d*, $J$ = 8.4) | 126.9 |
| $CF_3$ | – | – | – | – | – | 125.0 (*q*, $^{1}J$(C,F) = 272.0) |

all obtained 4-aryl-8-fluoro-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolines **5**–**7** have the relative configuration (3a*R**,4*S**,9b*S**).

In the next step, it was necessary to protect the *N*-atom of the tetrahydroquinoline core, because ozonolysis of **5**–**7** with a free amino group would lead to a complex mixture of unidentified products. *N*-Trifluoroacetyl derivatives **8**–**10** were obtained by the reaction of corresponding tetrahydroquinolines **5**–**7** with $(CF_3CO)_2O$ in the presence of $Et_3N$ in $CH_2Cl_2$ (*Scheme*).

According to the X-ray data of compound **10** (*Fig. 2*), the H-atoms at its stereogenic centers C(3a), C(4), and C(9b) are also *cis*-oriented with respect to each other. The similarity and convergence of main signals ($^1$H- and $^{13}$C-NMR) of compounds **8**–**10** evidence that all of them have the relative configuration (3a*R**,4*S**,9b*S**). The 4-Ar group in the crystal had a pseudo-axial orientation due to space barriers of the bulky *N*-trifluoroacetyl group, whereas, in amine **5**, the 4-Ar group is pseudo-equatorial.

Slow inversion between the conformers of heterocycles with the pseudo-axial and pseudo-equatorial 4-Ar group in compounds **8**–**10** with the bulky $CF_3CO$ group leads to a broadening of signals of H–C(3), H–C(3a), and H–C(9b) (*Table 2*), whereas in **5**–**7** the inversion is fast, and the signals of corresponding H-atoms have a well-resolved structure (*Table 1*).

The ozonolysis of *N*-trifluoroacetyl derivatives **8**–**10** in $CH_2Cl_2$ at 0° occured at the endocyclic C(1)=C(2) bond and led to the corresponding ozonides **11**–**13** (*Scheme*).

As noted earlier, according to the X-ray analysis, the formation of ozonides of substituted tetrahydrocyclopenta[*c*]quinolines occurs regio- and stereoselectively [12]. Instead of broadened signals of C(1) and C(2) in $^{13}$C-NMR spectra of the starting compounds ($\delta$(C) 128.8–130.6 ppm), spectra of the compounds **11**–**13b** contained narrow signals in the typical field for ozonides ($\delta$(C) 98.7–99.2 ppm) [12][13], confirming the transformation of the C=C bond into a 1,2,4-trioxolane ring. The cross-

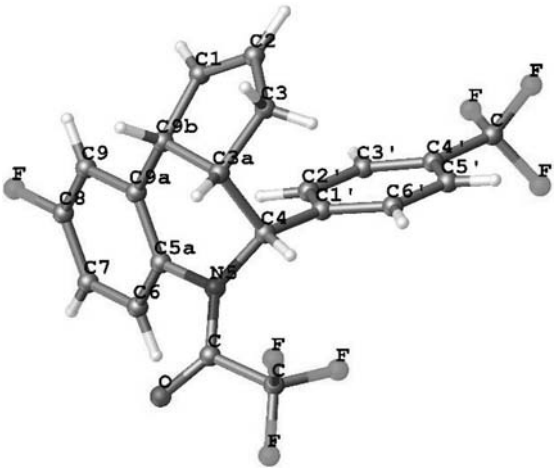



Fig. 2. *The molecular structure of 2,2,2-trifluoro-1-{(3a*R**,4*S**,9b*S**)-8-fluoro-3,3a,4,9b-tetrahydro-4-[4-(trifluoromethyl)phenyl]-5*H*-cyclopenta[c]quinolin-5-yl}ethanone* (**10**) *in the crystal.*

Table 2. *The $^{1}H$- and $^{13}C$-NMR Data* ($\delta$ in ppm, $J$ in Hz) *of Compounds* **8**–**10**

| Position | Compound **8** | | Compound **9** | | Compound **10** | |
|---|---|---|---|---|---|---|
| | $\delta$(H) | $\delta$(C) | $\delta$(H) | $\delta$(C) | $\delta$(H) | $\delta$(C) |
| 1 | 6.15 (br. *s*) | 130.5 | 6.44 (br. *s*) | 128.8 | 6.16 (br. *s*) | 130.6 |
| 2 | 5.84 (br. *s*) | 130.0 | 6.12 (br. *s*) | 129.0 | 5.85 (br. *s*) | 130.2 |
| 3 | 2.11 (br. *s*), 2.66 (br. *s*) | 35.6 | 2.09 (br. *s*), 2.64 (br. *s*) | 35.3 | 2.10 (br. *s*), 2.69 (br. *s*) | 35.6 |
| 3a | 3.63 (br. *s*) | 39.9 | 3.70 (br. *s*) | 40.1 | 3.69 (br. *s*) | 39.8 |
| 4 | 4.86 (br. *s*) | 58.4 | 5.01 (br. *s*) | 50.8 | 4.96 (br. *s*) | 58.2 |
| 5a | – | 137.6 | – | 138.9 | – | 138.6 |
| 6 | 6.67 (*d*, $J = 7.2$) | 116.4 (*d*, $^{3}J$(C,F) = 23.0) | 6.72 (*d*, $J = 7.6$) | 115.5 (*d*, $^{3}J$(C,F) = 23.0) | 6.87 (br. *s*) | 116.4 (*d*, $^{3}J$(C,F) = 23.0) |
| 7 | 6.88 (br. *s*) | 115.0 (*d*, $^{2}J$(C,F) = 17.0) | 6.89 (br. *s*) | 115.1 (*d*, $^{2}J$(C,F) = 15.0) | 7.06 (br. *s*) | 114.2 (*d*, $^{2}J$(C,F) = 17.0) |
| 8 | – | 162.6 (*d*, $^{1}J$(C,F) = 248.0) | – | 162.3 (*d*, $^{1}J$(C,F) = 248.0) | – | 161.8 (*d*, $^{1}J$(C,F) = 245.0) |
| 9 | 6.98 (*s*) | 114.0 (*d*, $^{2}J$(C,F) = 17.0) | 6.99 (*s*) | 113.9 (*d*, $^{2}J$(C,F) = 14.0) | 7.18 (*s*) | 113.9 (*d*, $^{2}J$(C,F) = 17.0) |
| 9a | – | 127.4 | – | 127.6 | – | 127.4 |
| 9b | 4.15 (br. *s*) | 46.6 | 4.12 (br. *s*) | 45.4 | 4.19 (br. *s*) | 45.6 |
| 1′ | – | 137.0 | – | 123.3 | – | 139.7 |
| 2′ | 7.17–7.19 (*m*) | 130.7 | – | 160.5 (*d*, $^{1}J$(C,F) = 245.0) | 7.00 (*d*, $J = 8.0$) | 129.4 |
| 3′ | – | 134.3 | 7.02–7.06 (*m*) | 114.8 | 7.37 (*d*, $J = 8.0$) | 125.0 |
| 4′ | 7.30–7.34 (*m*) | 127.9 | 7.16–7.18 (*m*) | 127.6 | – | 127.9 |
| 5′ | 7.04–7.06 (*m*) | 126.9 | 7.32–7.35 (*m*) | 127.6 | 7.37 (*d*, $J = 8.0$) | 125.2 |
| 6′ | 7.08–7.10 (*m*) | 129.5 | 7.36–7.37 (*m*) | 130.6 | 7.00 (*d*, $J = 8.0$) | 129.5 |
| $CF_3$ | – | – | – | – | – | 123.8 (*q*, $^{1}J$(C,F) = 272.0) |
| C=O | – | 156.7 (*q*, $^{3}J$(C,F) = 37.0) | – | 155.6 (*q*, $^{3}J$(C,F) = 37.0) | | 155.5 (*q*, $^{3}J$(C,F) = 37.0) |
| $CF_3$ | – | 116.3 (*q*, $^{1}J$(C,F) = 287.0) | – | 119.4 (*q*, $^{1}J$(C,F) = 287.0) | | 116.5 (*q*, $^{1}J$(C,F) = 287.0) |

Table 3. *The $^{1}H$- and $^{13}C$-NMR Data* ($\delta$ in ppm, $J$ in Hz) *of Ozonides* **11**–**13**

| Position | Compound **11** | | Compound **12** | | Compound **13** | |
|---|---|---|---|---|---|---|
| | $\delta$(H) | $\delta$(C) | $\delta$(H) | $\delta$(C) | $\delta$(H) | $\delta$(C) |
| 1 | 6.32 (br. *s*) | 98.7 | 6.42 (br. *s*) | 99.2 | 6.33 (br. *s*) | 98.8 |
| 4 | 5.84 (br. *s*) | 99.1 | 5.77 (br. *s*) | 99.2 | 5.83 (br. *s*) | 99.1 |
| 5 | 1.78–1.82 (*m*), 2.28–2.32 (*m*) | 30.2 | 1.99–2.15 (*m*), 2.29–2.35 (*m*) | 29.7 | 1.76–1.80 (*m*), 2.30–2.32 (*m*) | 30.1 |
| 5a | 3.28–3.31 (*m*) | 29.4 | 3.29–3.33 (*m*) | 31.8 | 3.33–3.37 (*m*) | 29.3 |
| 6 | 5.84 (*d*, $J$(6,5a) = 12.0) | 58.1 | 5.00 (*d*, $J$(6,5a) = 12.0) | 53.3 | 5.98 (*d*, $J$(6,5a) = 12.0) | 57.9 |
| 7a | – | 131.5 | – | 134.2 | – | 141.9 |
| 8 | 7.54–7.58 (*m*) | 122.7 (*d*, $^{3}J$(C,F) = 8.0) | 6.63–6.67 (*m*) | 123.5 (*d*, $^{3}J$(C,F) = 8.0) | 7.58 (*d*, $J$ = 8.0) | 116.5 (*d*, $^{3}J$(C,F) = 23.0) |
| 9 | 7.10–7.12(*m*) | 116.1 (*d*, $^{2}J$(C,F) = 23.0) | 6.85–6.89 (*m*) | 115.5 (*d*, $^{2}J$(C,F) = 22.0) | 7.00–7.10 (*m*) | 113.9 (*d*, $^{3}J$(C,F) = 24.0) |
| 10 | – | 160.5 (*d*, $^{1}J$(C,F) = 248.0) | – | 162.3 (*d*, $^{1}J$(C,F) = 242.0) | – | 160.2 (*d*, $^{1}J$(C,F) = 253.0) |
| 11 | 7.15 (*d*, $J$ = 8.8) | 116.1 (*d*, $^{2}J$(C,F) = 23.0) | 6.95–6.98 (*m*) | 114.0 (*d*, $^{2}J$(C,F) = 24.0) | 7.17 (*d*, $J$ = 8.0) | 113.7 (*d*, $^{2}J$(C,F) = 23.0) |
| 11a | – | 134.6 | – | 128.3 | – | 134.4 |
| 11b | 3.56 (*d*, $J$(11b,5a) = 10.8) | 38.6 | 3.54 (*d*, $J$(11b,5a) = 10.0) | 38.5 | 3.59 (*d*, $J$(11b,5a) = 10.8) | 38.6 |
| 1′ | – | 136.8 | – | 124.2 (*d*, $^{2}J$(C,F) = 3.0) | – | 138.9 |
| 2′ | 6.88–7.02 (*m*) | 130.4 | – | 159.7 (*d*, $^{1}J$(C,F) = 246.0) | 7.54–7.58 (*m*) | 130.0 |
| 3′ | – | 131.1 | 7.00–7.10 (*m*) | 116.2 (*d*, $^{2}J$(C,F) = 22.0) | 7.58–7.62 (*m*) | 125.1 |
| 4′ | 6.73 (*d*, $J$ = 7.6) | 127.5 | 7.11–7.15 (*m*) | 129.9 (*d*, $^{3}J$(C,F) = 6.0) | – | |
| 5′ | 7.19–7.21 (*m*) | 128.7 | 7.26–7.30 (*m*) | 130.4 (*d*, $^{3}J$(C,F) = 9.0) | 7.00–7.04 (*m*) | 126.0 |
| 6′ | 7.13–7.17 (*m*) | 129.4 | 7.32–7.38 (*m*) | 132.2 | 7.02–7.06 (*m*) | 130.4 |
| $CF_3$ | – | – | – | – | – | 122.5 (*q*, $^{1}J$(C,F) = 262.0) |
| C=O | | 155.5 (*q*, $^{2}J$(C,F) = 37.0) | | 155.7 (*q*, $^{2}J$(C,F) = 37.0) | | 155.6 (*q*, $^{2}J$(C,F) = 34.0) |
| $CF_3$ | | 115.8 (*q*, $^{1}J$(C,F) = 286.0) | | 117.9 (*q*, $^{1}J$(C,F) = 289.0) | | 117.9 (*q*, $^{1}J$(C,F) = 235.0) |

peak in the HMBC spectrum of ozonide **11** between the signal at $\delta$(C) 98.7 ppm and that at $\delta$(H) 3.56 (H–C(11b)) was unambiguously assigned to C(1), as well as a signal at ($\delta$(C) 99.1 ppm was attributed to C(4). Analogously, the significant signals of the tertiary C-atoms at $\delta$(C) 99.2 and 99.1 ppm for the ozonide cycle of **12** and **13** (*Table 3*) were assigned to C(4). Vicinal H-atoms at C(5a), C(6), and C(11b) of ozonides **11**–**13** were also *cis*-oriented relative to each other. This was suggested by their spin-spin coupling constants ($J$(6,5a) = 12, $J$(11b,5a) = 10.0–10.8 Hz). The $[M-H]^-$ ion peaks in ESI mass spectra of **11**–**13** provided their molecular weights. According to $^1$H- and $^{13}$C-NMR spectra, and the X-ray diffraction data reported earlier for related ozonides [10][12], the newly obtained ozonides **11**–**13** were identified as (1*R**,4*S**,5a*R**,6*S**,11b*S**)-6-aryl-10-fluoro-4,5,5a,6,7,11b-hexahydro-7-(trifluoroacetyl)-1*H*-1,4-epoxy-[1,2]dioxepino[5,4-*c*]quinolines (*Table 3*).

In conclusion, the new 4-aryl-8-fluoro-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolines were synthesized by an effective one-pot three-component cyclocondensation of 4-fluoroaniline with an aromatic aldehydes and cyclopentadiene. Their subsequent *N*-trifluoroacetylation and ozonolysis furnished new stable ozonides with a tetrahydroquinoline core.

This work was financially supported by *Russian Fond of Basic Researches* (Grant 14-03-00286) and by the *Program Presidium of Russian Academy Sciences.*

## Experimental Part

*General*. The starting compounds were purchased from *Acros Organics*. Column chromatography (CC) and TLC: silica gel (< 0.06 mm) and pre-coated silica gel plates (*Silufol*), resp.; visualization with the $I_2$ vapor. M.p.: *Boetius* hot-stage microscope. 1D- ($^1$H and $^{13}$C) and 2D- (COSY, NOESY, HSQC, and HMBC) NMR spectra: of *Bruker Avance-400* spectrometer (400.1 ($^1$H) and 100.6 MHz ($^{13}$C)), equipped with broadband observer probe; all recordings were set up with standard *Bruker* methods; chemical shifts in ppm with TMS as the internal standard. Electrospray ionization (ESI) MS: of HPLC mass spectrometer *LCMS-2010EV* (*Shimadzu*) in the negative-ion mode at the corona discharge needle ionizing electrode and ionizing cap potential of 4.5 kV and −3.5 kV, resp.; the temp. and voltage of the interface capillary under APCI (ESI) conditions, 230° and 5 (25) to −5 (−25) V, resp.; the nebulizer gas ($N_2$) low rate, 0.5 (1.5) l/min; the high-frequency lenses (Q-array) voltage, 5 to −5 V; sample soln. (direct syringe sample inlet) under APCI (ESI) conditions, in MeOH (MeCN); mobile phase, MeOH (MeCN/$H_2O$, 75/25); the mobile phase flow rate, 20 (50) µl/min. Elemental analyses: *Carlo Erba EA-1108 CHNS-O* analyzer.

*X-Ray Crystal-Structure Determination*. Single crystals of **5** and **10** were grown from hexane/AcOEt 1:1 at r.t. X-Ray diffraction data were collected on a *XCalibur Eos* diffractometer with graphite monochromated Mo$K_\alpha$ radiation ($\lambda$ 0.71073 Å). Collection and processing of data was performed by using the program CrysAlis$^{Pro}$, *Oxford Diffraction Ltd.*, Version 1.171.36.28. The structure was solved by direct methods as implemented in the program SHELXS-97 [14]. The refinement was carried out using SHELXL-97 [15]. The structure was refined by a full-matrix least-squares technique using anisotropic thermal parameters for non-H-atoms and a riding model for H-atoms. The X-ray crystallographic data have been deposited with the *Cambridge Crystallographic Data Center* (*CCDC*).

*Crystal Data of* **5**. $C_{18}H_{14}FClN$, $M_r$ 300.77, triclinic, $P\bar{1}$ (No. 2), $a$ = 9.2503(11) Å, $b$ = 9.7262(12) Å, $c$ = 9.9834(14) Å, $\alpha$ = 114.029(13)°, $\beta$ = 104.198(12)°, $\gamma$ = 104.749(11)°, $V$ = 728.81(16) Å$^3$, $T$ = 293.(2) K, $D_{calc}$ = 1.371 mg/mm$^3$, $Z$ = 2; reflections collected, 5244; independent reflections, 3685 ($R$(int) = 0.0147), $R$ = 0.047, $R_w$ = 0.162; goodness-of-fit, 0.915; CCDC-970716.

*Crystal Data of* **10**. $C_{21}H_{14}NOF_7$, $M_r$ = 410.33, triclinic, $P\bar{1}$ (No. 2), $a$ = 9.5321(8) Å, $b$ = 10.3404(8) Å, $c$ = 10.8512(11) Å, $\alpha$ = 117.330(9)°, $\beta$ = 100.176(8)°, $\gamma$ = 91.626(7)°, $V$ = 927.86(14) Å$^3$,

$T = 293.(2)$ K, $D_{calc} = 1.469$ mg/mm$^3$, $Z = 2$; reflections collected, 4387; independent reflections, 3099 ($R$(int) = 0.0091), $R = 0.047$, $R_w = 0.137$; goodness-of-fit 1.058; CCDC-964374. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data_request/cif.

*General Procedure of Synthesis 4-Aryl-8-fluoro-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[c]quinolines* **5**–**7**. $CF_3COOH$ 0.23 ml (3 mmol) was added to a soln. of *4-fluoroaniline* (**1**, 0.38 ml, 3.0 mmol) in anh. MeCN (20 ml), followed by an addition of freshly distilled cyclopentadiene (1.23 ml, 15 mmol) at 0 and aldehyde **2** (**3** or **4**) (3 mmol). The mixture was stirred for 0.5 h until starting **1** disappeared (TLC monitoring, hexane/AcOEt 3:1). The solvent was evaporated, and the residue was diluted with sat. aq. $NaHCO_3$ and extracted with AcOEt. The org. layer was concentrated and the residue was subjected to CC (hexane).

rel-*(3a*R*,4*S*,9b*S*)-4-(3-Chlorophenyl)-8-fluoro-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline* (**5**). Yield: 80%. $R_f$ (hexane/AcOEt 3:1) 0.69 . M.p. 88–90° (from hexane). $^1$H- and $^{13}$C-NMR: see *Table 1*. MALDI-TOF-MS: 300 ($M + H^+$). Anal. calc. for $C_{18}H_{15}ClFN$ (299.77): C 72.12, H 5.04, N 4.67; found: C 72.32, H 5.21, N, 4.76.

rel-*(3a*R*,4*S*,9b*S*)-8-Fluoro-4-(2-fluorophenyl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline* (**6**). Yield: 86%. $R_f$ (hexane/AcOEt 3:1) 0.62. M.p. 60–62° (from hexane). $^1$H- and $^{13}$C-NMR: see *Table 1*. MALDI-TOF-MS: 283 ($[M]^+$). Anal. calc. for $C_{18}H_{15}F_2N$ (283.32): C 76.31, H 5.34, N 4.94; found: C 76.48, H 5.26, N 4.73.

rel-*(3a*R*,4*S*,9b*S*)-8-Fluoro-3a,4,5,9b-tetrahydro-4-[4-(trifluoromethyl)phenyl]-3*H*-cyclopenta[*c*]-quinoline* (**7**). Yield: 96%. $R_f$ (hexane/AcOEt 3:1) 0.70. M.p. 74–76° (from hexane). $^1$H- and $^{13}$C-NMR: see *Table 1*. MALDI-TOF-MS: 332 ($[M - H]^+$). Anal. calc. for $C_{19}H_{15}F_4N$ (333.32): C 68.46, H 4.54, N 4.20; found: C 68.98, H 4.58, N 4.33.

*General Procedure for the Synthesis of 4-Aryl-8-fluoro-3,3a,4,9b-tetrahydro-5*H*-cyclopenta[c]quinolin-5-yl]-2,2,2-trifluoroethanones* **8**–**10**. $(CF_3CO)_2O$ (0.34 ml, 2.4 mmol) and 0.33 ml (2.4 mmol) of $Et_3N$ were added to a soln. of 2.0 mmol of **5** (**6** or **7**) in 10 ml of $CH_2Cl_2$. The mixture was stirred, until the starting was completely consumed (TLC), and poured into cold $H_2O$ (5 ml). The product was extracted with $CH_2Cl_2$ (20 ml), and the extract was washed with a sat. aq. $NaHCO_3$ and then NaCl. The org. layer was concentrated, and the residue was subjected to CC (hexane).

rel-*1-[(3a*R*,4*S*,9b*S*)-4-(3-Chlorophenyl)-8-fluoro-3,3a,4,9b-tetrahydro-5*H*-cyclopenta[*c*]quinolin-5-yl]-2,2,2-trifluoroethanone* (**8**). Amorphous. Yield: 97%. $R_f$ (hexane/AcOEt 3:1) 0.61. $^1$H- and $^{13}$C-NMR: see *Table 2*. MALDI-TOF-MS: 418 ($[M + Na]^+$). Anal. calc. for $C_{20}H_{14}ClF_4NO$ (395.78): C 60.69, H 3.57, N 3.54; found: C 60.62, H 3.35, N 3.65.

rel-*2,2,2-Trifluoro-1-[(3a*R*,4*S*,9b*S*)-8-fluoro-4-(2-fluorophenyl)-3,3a,4,9b-tetrahydro-5*H*-cyclopenta[*c*]quinolin-5-yl]ethanone* (**9**). Amorphous Yield: 97%. $R_f$ (hexane/AcOEt 3:1) 0.60. $^1$H- and $^{13}$C-NMR: see *Table 2*. MALDI-TOF-MS: 378 ($[M - H]^-$). Anal. calc. for $C_{20}H_{14}F_5NO$ (379.32): C 63.32, H 3.72, N 3.69; found: C 63.53, H 3.85, N 3.74.

rel-*2,2,2-Trifluoro-1-{(3a*R*,4*S*,9b*S*)-8-fluoro-3,3a,4,9b-tetrahydro-4-[4-(trifluoromethyl)phenyl]-5*H*-cyclopenta[*c*]quinolin-5-yl}ethanone* (**10**). Yield: 95%. $R_f$ (hexane/AcOEt 3:1) 0.61. M.p. 90–92° (from hexane). $^1$H- and $^{13}$C-NMR: see *Table 2*. MALDI-TOF-MS: 430 ($[M + H]^+$). Anal. calc. for $C_{21}H_{14}F_7NO$ (429.33): C 58.75, H 3.29, N 3.26; found: C 58.65, H 3.25, N 3.34.

*General Procedure for the Synthesis of 1-[6-Aryl-10-fluoro-1,4,5,5a,6,11b-hexahydro-7*H*-1,4-epoxy[1,2]dioxepino[5,4-c]quinolin-7-yl]-2,2,2-trifluoroethanones* **11**–**13**. The $O_2/O_3$ mixture (the ozonator productivity was 30 mmol $O_3$/h) was passed through a soln. of **8** (**9** or **10**) (1.5 mmol in $CH_2Cl_2$ (20 ml)) at 0° with stirring, until the starting compound disappeared (*ca.* 3 min, TLC monitoring ($CHCl_3$)). The mixture was purged with Ar and concentrated. The residue was subjected to CC ($CHCl_3$).

rel-*1-[(1*R*,4*S*,5a*R*,6*S*,11b*S*)-6-(3-Chlorophenyl)-10-fluoro-1,4,5,5a,6,11b-hexahydro-7*H*-1,4-epoxy[1,2]dioxepino[5,4-c]quinolin-7-yl]-2,2,2-trifluoroethanone* (**11**). Yield: 65%. M.p. 90–92° (from hexane). $^1$H- and $^{13}$C-NMR: see *Table 3*. ESI-MS: 443 ($[M]^+$).

rel-*2,2,2-Trifluoro-1-[(1*R*,4*S*,5a*R*,6*S*,11b*S*)-10-fluoro-6-(2-fluorophenyl)-1,4,5,5a,6,11b-hexahydro-7*H*-1,4-epoxy[1,2]dioxepino[5,4-c]quinolin-7-yl]ethanone* (**12**). Yield: 68%. M.p. 115–116° (from hexane). $^1$H- and $^{13}$C-NMR: see *Table 3*. ESI-MS: 426 ($[M - H]^-$).

rel-*2,2,2-Trifluoro-1-{(1*R*,4*S*,5a*R*,6*S*,11b*S*)-10-fluoro-1,4,5,5a,6,11b-hexahydro-6-[4-(trifluoromethyl)phenyl]-7*H*-1,4-epoxy[1,2]dioxepino[5,4-c]quinolin-7-yl}ethanone* (**13**). Yield: 60%. M.p. 49–51° (from hexane). $^1$H- and $^{13}$C-NMR: see *Table 3*. ESI-MS: 476 ($[M-H]^-$).

## REFERENCES


[1] V. A. Petrov, 'Fluorinated Heterocyclic Compounds: Synthesis, Chemistry, and Applications', John Wiley & Sons, Inc., Hoboken, USA, 2009.
[2] R. Filler, R. Saha, *Future Med. Chem.* **2009**, *1*, 777.
[3] A. R. Ronald, D. E. Low, 'Fluoroquinolone Antibiotics', Birkhäuser Verlag AG, Basel, 2003.
[4] M. S. T. Makki, D. A. Bakhotmah, R. M. Abdel-Rahman, *Int. J. Org. Chem.* **2012**, *2*, 49.
[5] P. C. Sharma, A. Jain, S. Jain, *Acta Pol. Pharm. Drug Res.* **2009**, *66*, 587.
[6] L. S. Povarov, *Usp. Khim.* **1967**, *36*, 1533.
[7] V. A. Glushkov, A. G. Tolstikov, *Usp. Khim.* **2008**, *77*, 138.
[8] P. A. Grieco, A. Bahsas, *Tetrahedron Lett.* **1988**, *29*, 5855.
[9] A. S. Kiselyov, L. Smith II, R. W. Armstrong, *Tetrahedron* **1998**, *54*, 5089.
[10] A. G. Tolstikov, R. G. Savchenko, D. V. Nedopekin, S. R. Afon'kina, E. S. Lukina, V. N. Odinokov, *Izv. Akad. Nauk. Ser. Khim.* **2011**, *60*, 153.
[11] G. A. Tolstikov, A. G. Tolstikov, O. V. Tolstikova, *Usp. Khim.* **1996**, *65*, 836.
[12] S. Kawamura, R. Takeuchi, A. Masuyama, M. Nojima, K. J. McCullough, *J. Org. Chem.* **1998**, *63*, 5617.
[13] A. G. Tolstikov, L. M. Khalilov, R. G. Savchenko, D. V. Nedopekin, V. A. Glushkov, G. F. Krainova, I. V. Glukhov, M. Y. Antipin, V. N. Odinokov, *Izv. Akad. Nauk. Ser. Khim.* **2009**, *58*, 1929.
[14] G. M. Sheldrick, *Acta Cryst., Sect. A* **2008**, *64*, 112.
[15] G. M. Sheldrick, SHELXL-97 Program for the Solution and Refinement of X-Ray Crystal Structures, University of Göttingen, 1997.


*Received December 25, 2013*