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Search of Synthetic Approaches to 1, 3, 4-Oxadiazoles with 1, 2, 2-Trimethylcyclopentane Moiety

Ye O Tsapko

Abstract
The work continues our research that deals with the search of biologically active compounds that are camphoric acid derivatives and dedicated to the synthesis of its new derivatives containing 1,3,4-oxadiazole cycle. To achieve this goal, at the first stage N'-aroylhydrazides of (±)-camphoric and (±)-cis-3-dichloromethyl-1,2,2-trimethylcyclopentancarboxylic acids were synthesized by acylation of aromatic acids hydrazides. It was established that dehydration of the obtained hydrazides of (±)-camphoric acid ended up with closure of imide cycle and formation of N-[(1S,5R),(1R,5S)-1,8,8-trimethyl-2,4-dioxo-3-azabicyclo[3.2.1]oct-3-yl]benzamides. The target 1,3,4-oxadiazoles with 1,2,2-trimethylcyclopentane moiety were managed to obtain from N'-aroylhydrazides of (±)-cis-3-dichloromethyl-1,2,2-trimethyl-cyclopentancarboxylic acid.

Keywords: (±)-cis-3-dichloromethyl-1,2,2-trimethylcyclopentancarboxylic acid; camphoric acid; hydrazides; 1,3,4-oxadiazoles.

Introduction
(±)-Cis-camphoric acid is the known compound of semi-synthetic origin which introduction in molecules of new substances reduces their toxicity and improves bioavailability. In previous studies camphoric acid derivatives containing heterocyclic residues such as quinazolone-4, furan and thiophene have been obtained. The results of pharmacological studies revealed that they had diuretic [1, 2], hypoglycemic [3, 4] and anticonvulsant activity [5]. These data allow us to consider derivatives of camphoric acid as promising objects for further studies with the purpose of new medicinal substances development. To reach such a goal, the variety of camphoric acid derivatives have been enlarged with new compounds bearing 1,3,4-oxadiazole moiety. The introduction of this heterocyclic pharmacophore may potentially lead to compounds with new types of biological activity, because 1,3,4-oxadiazoles are reviewed as compounds with antiproliferative [6], anticonvulsant [7], anti-inflammatory [8, 9], antimicrobial [10] and other activities.

Results and Discussion
The formation of oxadiazole cycle via heterocyclization of hydrazides is the widely used approach in modern chemistry [11]. Therefore, to synthesize the intermediate reagent for new oxadiazoles with 1,2,2-trimethylcyclopentane moiety the acylation of aromatic acid hydrazides 2a-d with (±)-camphoric acid anhydride have been carried out at first stage. As a result, (1R,3S),(1S,3R)-1,2,2-trimethyl-3-{[2-(R-benzoyl)hydrazinyl]carbonyl}cyclopentane-carboxylic acids 3a-d were obtained in high yields (85-94%) (Fig. 1). The structure of the synthesized compounds 3a-d was confirmed by elemental analysis and ^{1}H NMR spectroscopy. It should be noted that characteristic feature of the ^{1}H NMR spectra of the acids 3a-d is the signals of two NH-protons and protons of two methyl groups of cyclopentane moiety that are splitted into two singlets.

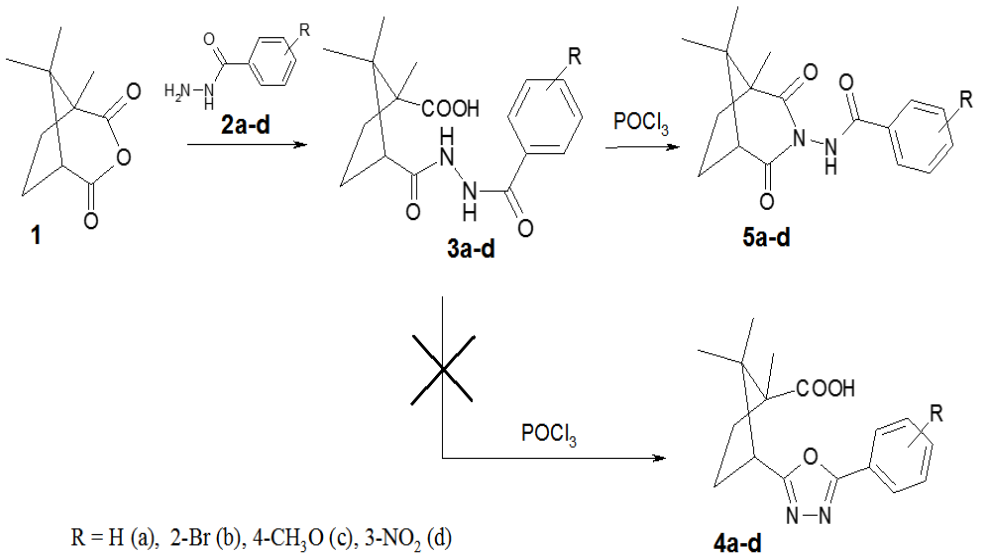

Fig 1

Dehydration of the acids 3a-d under treatment with phosphorous oxychloride does not follow in the desired direction of formation (1R,3S),(1S,3R)-1,2,2-trimethyl-3-(5-R-1,3,4-oxadiazol-2-yl)cyclopentancarboxylic acids 4a-d, but it ends up with closure of camphorimide cycle and formation of N-(1,8,8-trimethyl-2,4-dioxo-3-azabicyclo[3.2.1]oct-3-yl)benzamides 5a-d as products. The same result was obtained when another dehydrating reagents (e.g., polyphosphoric acid, thionyl chloride) were used. Unlike the ^{1}H NMR spectra of the acid 3a-d, in the spectra of the benzamides 5a-d multiplicity of proton signal of H-3 of cyclopentane moiety has changed, namely, multiplet turned into doublet and shifted in weak fields (about 0.1 ppm). As well, singlet splitting of one methyl group disappeared.

Given the impossibility to obtain target compounds based on N'-aroylhydrazides of (±)-camphoric acid 3a-d, to achieve the goal on the synthesis of 1,3,4-oxadiazole derivatives we used another starting reagent – (±)-cis-3-dichloromethyl-1,2,2-trimethylcyclopentancarboxylic acid 6 (fig. 2). The acid 6 was prepared from racemic camphor by its treatment with potassium hydroxide in tetrachloromethane in the presence of tert-butanol [12]. As a next step, the acid 6 was converted into (±)-cis-3-dichloromethyl-1,2,2-trimethylcyclopentancarbonyl chloride 7 using thionyl chloride in anhydrous dioxane. The process was monitored by TLC until exhaustion of the initial compounds, and it have taken 3 h to complete the reaction; such a long time of the process could be explained by the steric hindrance of the carboxylic group of acid 6. The product 7 was used for acylation of hydrazides 2a-d without preliminarily isolation. As a result, N'-{[(1S,3R),(1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]carbonyl}benzo-hydrazides 8a-d were obtained. Further dehydration of the compounds 8a-d via treatment with phosphorous oxychloride have led to the target 2-[(1S,3R),(1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]-5-(R-phenyl)-1,3,4-oxadiazoles 9a-d (Method A). Oxadiazoles 9a-d were also obtained in a single step starting from the acid 6 (Method B); this pathway gives the higher yields than the two-steps procedure of Method A.

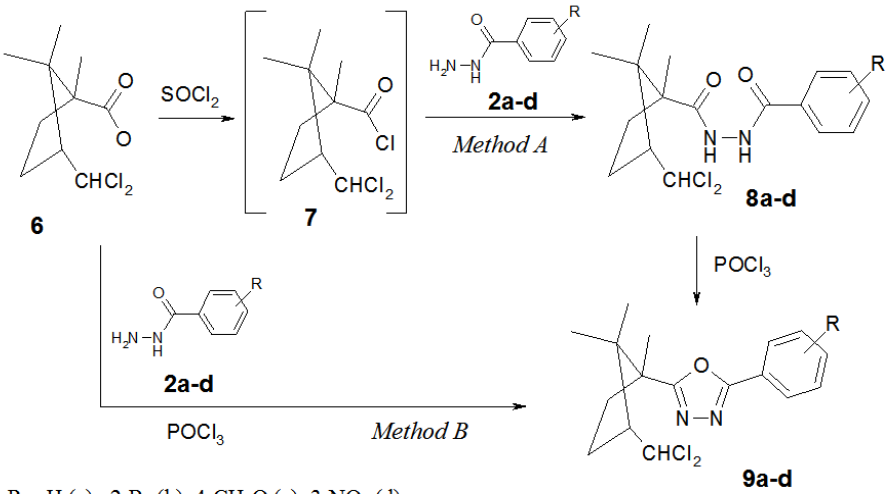

Fig 2

Hydrolysis on dichloromethyl group of the compounds 9a-d could have opened the way to camphoric acid derivatives with 1,3,4-oxadizole moiety. But according to the results obtained, the products 9a-d were stable under hydrolysis, and the only starting compounds 9a-d were isolated after their boiling in with aqueous-alcoholic solution of potassium hydroxide for 24h.

Materials and Methods

^{1}H NMR spectra were recorded on a Varian Mercury VX-200 (200 MHz) spectrometer in DMSO-d_6 solutions with TMS as an internal standard. Elemental analysis was performed on EuroVector EA-3000 microanalyzer. Melting points were determined on a Kofler bench. The purity determination of the substrates accomplished by TLC on silica-gel Silufol UV_{254} plates and using chloroform-dioxane (4:1 v/v) and chloroform-propanol-2 (3:2 v/v) as eluents.

General procedure of synthesis of *(1R,3S),(1S,3R)-3-[(2-R-benzoylhydrazinyl)carbonyl]-1,2,2-trimethylcyclopentanecarboxylic acid* (3a-d). Dissolve 1,8g (0,01 mol) of (±)-camphoric anhydride 1 in 10 ml of propanol-1, add 0,011mol of the corresponding hydrazide 2 and heat under the reflux for 1 h. Cool the solution, add water to initiate crystallization. The precipitate formed is filtered off and recrystallized from aqueous ethanol.

(1R,3S),(1S,3R)-3-[(2-benzoylhydrazinyl)carbonyl]-1,2,2-trimethylcyclopentanecarboxylic acid 3a. The yield is 93%. M.p. 173-174°C. Found, %: C 67.29, H 7.11, N 9.03. $C_{17}H_{22}N_2O_4$. Calculated, %: C 64.13, H 6.97, N 8.80. ^{1}H NMR, δ, ppm: 0.78, 0.82ds (3H, CH_3), 1.14, 1.19ds (3H, CH_3), 1.26s (3H, CH_3), 1.32-1.50m (1H, CH_2CH_2), 1.59-1.85m (1H, CH_2CH_2), 1.91-2.13m (1H, CH_2CH_2), 2.34-2.58m (1H, CH_2CH_2), 2.66-2.81m (1H, CH), 7.42-7.60m (3H, H-3,4,5), 7.82-7.90m (2H, H-2,6), 9.36, 9.62ds (1H, NH), 10.16, 10.27ds (1H, NH), 12.10bs (1H, COOH).

(1R,3S),(1S,3R)-3-{[2-(2-bromobenzoyl)hydrazinyl]carbonyl}-1,2,2-trimethylcyclopentanecarboxylic acid 3b. The yield is 90%. M.p. 187-188°C. Found, %: C 51.38, H 5.22, N 7.23. $C_{17}H_{21}BrN_2O_4$. Calculated, %: C 51.40, H 5.33, N 7.05. ^{1}H NMR, δ, ppm: 0.50s (3H, CH_3), 0.86s (3H, CH_3), 0.94s (3H, CH_3), 1.03-1.22m (1H, CH_2CH_2), 1.31-1.56m (1H, CH_2CH_2), 1.63-1.83m (1H, CH_2CH_2), 2.05-2.24m (1H, CH_2CH_2), 2.38-2.53m (1H, CH), 6.93-7.24m (3H, H-3,4,5), 7.39d (1H, H-6, J=7.3 Hz), 9.19, 9.48ds (1H, NH), 9.74, 9.89ds (1H, NH), 11.52bs (1H, COOH).

(1R,3S),(1S,3R)-1,2,2-trimethyl-3-{[2-(3-nitrobenzoyl)hydrazinyl]carbonyl}cyclopentanecarboxylic acid 3c. The yield is 85%. M.p. 207-208°C. Found, %: C 59.19, H 5.99, N 11.71. $C_{17}H_{21}N_3O_6$. Calculated, %: C 59.16, H 5.83, N 11.56. ^{1}H NMR, δ, ppm: 0.78, 0.82ds (3H, CH_3), 1.15, 1.19ds (3H, CH_3), 1.25s (3H, CH_3), 1.32-1.50m (1H, CH_2CH_2), 1.61-1.83m (1H, CH_2CH_2), 1.91-2.08m (1H, CH_2CH_2), 2.34-2.58m (1H, CH_2CH_2), 2.66-2.84m (1H, CH), 7.81t (1H, H-5, J=8.1 Hz), 8.30d (1H, H-6, J=8.1 Hz), 8.42d (1H, H-4, J=8.1 Hz), 8,69s (1H, H-2), 9.50, 9.79ds (1H, NH), 10.61, 10.69ds (1H, NH), 11.75brs (1H, COOH).

(1R,3S),(1S,3R)-3-{[2-(4-methoxybenzoyl)hydrazinyl]carbonyl}-1,2,2-trimethylcyclopentanecarboxylic acid 3d. The yield is 94%. M.p. 183-184°C. Found, %: C 62.01, H 6.83, N 8.19. $C_{18}H_{24}N_2O_5$. Calculated, %: C 62.05, H 6.94, N 8.06. ^{1}H NMR, δ, ppm: 0.78, 0.82ds (3H, CH_3O), 1.15, 1.18ds (3H, CH_3), 1.26s (3H, CH_3), 1.32-1.51m (1H, CH_2CH_2), 1.57-1.82m (1H, CH_2CH_2), 1.89-2.12m (1H, CH_2CH_2), 2.32-2.51m (1H, CH_2CH_2), 2.65-2.82m (1H, CH), 7.00d (2H, H-3,5, J=8.6 Hz), 7.85d (2H, H-2,6, J=8.6 Hz), 9.29, 9.54ds (1H, NH), 10.03, 10.11ds (1H, NH), 11.70brs(1H, COOH).

General procedure of synthesis of *N-(1,8,8-trimethyl-2,4-dioxo-3-azabicyclo[3.2.1]oct-3-yl)benzamides* 5a-d. Heat the mixture of 0.01 mol of the corresponding acid 3 and 5 ml (0.02 mol) of phosphorous oxychloride under the reflux with stirring at 80°C for 1 h. Cool the mixture and add crushed ice. The precipitate formed is filtered off, washed with water, then with 10% sodium bicarbonate solution, and again with water and crystallized from aqueous ethanol.

N-[(1*S*,5*R*),(1*R*,5*S*)*-1,8,8-trimethyl-2,4-dioxo-3-azabicyclo[3.2.1]oct-3-yl]benzamide* 5a. The yield is 81%. M.p. 163-164°C. Found, %: C 67.94, H 6.77, N 9.47. $C_{17}H_{20}N_2O_3$. Calculated, %: C 67.98, H 6.71, N 9.33. ^{1}H NMR, δ, ppm: 0.96, 1.01ds (3H, CH_3), 1.13s (3H, CH_3), 1.24s (3H, CH_3), 1.56-2.12m (3H, CH_2CH_2), 2.17-2.39m (1H, CH_2CH_2), 2.81d (1H, CH, J=7.0 Hz), 7.48-7.62m (3H, H-3,4,5), 7.82-8.87m (2H, H-2,6), 10.51, 10.64ds (1H, NH).

2-Bromo-N-[(1*S*,5*R*),(1*R*,5*S*)*-1,8,8-trimethyl-2,4-dioxo-3-azabicyclo[3.2.1]oct-3-yl]benzamide* 5b. The yield is 73%. M.p. 210-211°C. Found, %: C 54.00, H 5.12, N 7.48. $C_{17}H_{19}BrN_2O_3$. Calculated, %: C 53.84, H 5.05, N 7.39. ^{1}H NMR, δ, ppm: 0.96s (3H, CH_3), 1.14s (3H, CH_3), 1.23s (3H, CH_3), 1.57-2.11m (3H, CH_2CH_2), 2.16-2.38m (1H, CH_2CH_2), 2.81d (1H, CH, J=7.0 Hz), 7.35-7.55m (3H, H-3,4,5), 7.71d (1H, H-6, J=7.0 Hz), 10.56, 10.73ds (1H, NH).

3-Nitro-N-[(1*S*,5*R*),(1*R*,5*S*)*-1,8,8-trimethyl-2,4-dioxo-3-azabicyclo[3.2.1]oct-3-yl]benzamide* 5c. The yield is 69%. M.p. 186-187°C. Found, %: C 59.21, H 5.71, N 12.32. $C_{17}H_{19}N_3O_5$. Calculated, %: C 59.12, H 5.55, N 12.17. ^{1}H NMR, δ, ppm: 0.97, 1.02ds (3H, CH_3), 1.14s (3H, CH_3), 1.25s (3H, CH_3), 1.57-2.11m (3H, CH_2CH_2), 2.17-2.41m (1H, CH_2CH_2), 2.83d (1H, CH, J=7.0 Hz), 7.85t (1H, H-5, J=8.1 Hz), 8.30d (1H, H-6, J=8.1 Hz), 8.47d (1H, H-4, J=8.1 Hz), 8.66-8.74m (1H, H-2), 11.11, 11.27ds (1H, NH).

4-Methoxy-N-[(1*S*,5*R*),(1*R*,5*S*)*-1,8,8-trimethyl-2,4-dioxo-3-azabicyclo[3.2.1]oct-3-yl]benzamide* 5d. The yield is 80%. M.p. 198-199°C. Found, %: C 65.40, H 6.80, N 8.56. $C_{18}H_{22}N_2O_4$. Calculated, %: C 65.44, H 6.71, N 8.48. ^{1}H NMR, δ, ppm: 0.95, 1.01ds (3H, CH_3), 1.12s (3H, CH_3), 1.25s (3H, CH_3), 1.59-2.11m (3H, CH_2CH_2), 2.16-2.36m (1H, CH_2CH_2), 2.79d (1H, CH, J=7.0 Hz), 7.05d (2H, H-3,5, J=8.8 Hz), 7.85d (2H, H-2,6, J=8.8 Hz), 10.47, 10.62ds (1H, NH).

General procedure of synthesis of N'-{[(1S,3R),(1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]carbonyl}benzohydrazides 8a-d. Dissolve 2.4g (0.01 mol) of (±)-cis-3-dichloromethyl-1,2,2-trimethylcyclopentancarboxylic acid 6 in 10 ml of anhydrous dioxane, add 2.2 ml (0.011 mol) of thionyl chloride. Heat the mixture under the reflux for 3 h. To the obtained solution add 0.01 mol of the corresponding hydrazide 2 in 5-10 ml of anhydrous dioxane under stirring and heat for 30 min. Cool the mixture, add water to initiate crystallization. The precipitate formed is filtered off and recrystallized from aqueous ethanol.

N'-{[(1S,3R),(1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]carbonyl}benzohydrazide 8a. The yield is 70%. M.p. 95-96°C. Found, %: C 57.16, H 6.31, N 7.92. $C_{17}H_{22}Cl_2N_2O_2$. Calculated, %: C 57.15, H 6.21, N 7.84. ^{1}H NMR, δ, ppm:0.91s (3H, CH_3), 1.19s (3H, CH_3), 1.29s (3H, CH_3), 1.33-1.50m (1H, CH_2CH_2), 1.60-1.80m (1H, CH_2CH_2), 1.94-2.11m (1H, CH_2CH_2), 2.26-2.62m (2H, CH, CH_2CH_2),

6,27d (1H, $CHCl_2$, J=8.8 Hz), 7.47-7.60m (3H, H-3,4,5), 7.86d (2H, H-2,6, J=8.1 Hz), 9.36s (1H, NH), 10.16s (1H, NH).

2-Bromo-N'-{[(1S,3R),(1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]carbonyl}benzohydrazide 8b. The yield is 72%. M.p. 202-203°C. Found, %: C 46.75, H 4.82, N 6.56. $C_{17}H_{21}BrCl_2N_2O_2$. Calculated, %: C 46.81, H 4.85, N 6.42. ^{1}H NMR, δ, ppm: 0.91s (3H, CH_3), 1.19s (3H, CH_3), 1.29s (3H, CH_3), 1.33-1.50m (1H, CH_2CH_2), 1.60-1.61m (1H, CH_2CH_2), 1.94-2.11m (1H, CH_2CH_2), 2.26-2.62m (2H, CH, CH_2CH_2), 6.27d (1H, $CHCl_2$, J=8.8 Hz), 7.32-7.51m (3H, H-3,4,5), 7.66d (1H, H-6, J=7.3), 9.36s (1H, NH), 10.16s (1H, NH).

N'-{[(1S,3R),(1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]carbonyl}-3-nitrobenzohydrazide 8c. The yield is 66%. M.p. 153-154°C. Found, %: C 50.84, H 5.18, N 10.58. $C_{17}H_{21}Cl_2N_3O_4$. Calculated, %: C 50.76, H 5.26, N 10.45. ^{1}H NMR, δ, ppm: 0.91s (3H, CH_3), 1.20s (3H, CH_3), 1.29s (3H, CH_3), 1.32-1.52m (1H, CH_2CH_2), 1.54-1.81m (1H, CH_2CH_2), 1.89-2.14m (1H, CH_2CH_2), 2.25-2.51m (2H, CH, CH_2CH_2), 6,28d (1H, $CHCl_2$, J=8.8 Hz), 7.76-7.89m (1H, H-5), 8.27-8.51m (2H, H-4,6), 8,67-8,75m (1H, H-2), 9.54s (1H, NH), 10.62s (1H, NH).

N'-{[(1S,3R),(1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]carbonyl}-4-methoxybenzohydrazide 8d. The yield is 70%. M.p. 161-162°C. Found, %: C 55.69, H 6.20, N 7.40. $C_{17}H_{21}Cl_2N_3O_4$. Calculated, %: C 55.82, H 6.25, N 7.23. ^{1}H NMR, δ, ppm: 0.91s (3H, CH_3), 1.19s (3H, CH_3), 1.29s (3H, CH_3), 1.33-1.51m (1H, CH_2CH_2), 1.58-1.80m (1H, CH_2CH_2), 1.87-2.10m (1H, CH_2CH_2), 2.26-2.54m (2H, CH, CH_2CH_2), 6,27d (1H, $CHCl_2$, J=8.8 Hz), 7.06d (2H, H-3,5, J=8.6 Hz), 7.86d (2H, H-2,6, J=8.6 Hz), 9.35s (1H, NH), 10.14s (1H, NH).

General procedure of synthesis of 2-[3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]-5-R-phenyl-1,3,4-oxadiazoles 9a-d.

Method A: Heat 0.01 mol of N'-{[(1S, 3R), (1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]carbonyl}benzohydrazide 8 and 5 ml (0.02 mol) of phosphorous oxychloride under the reflux with stirring at 80ºC for 1 h. Cool the mixture and add crushed ice. The precipitate formed is filtered off, washed with water, then with 10% sodium bicarbonate solution, and again with water and crystallized from aqueous ethanol.

Method B: Heat 2.4g (0.01 mol) of (±)-cis-3-dichloromethyl-1,2,2-trimethylcyclopentancarboxylic acid 6, 0.01 mol of the corresponding hydrazide 2 and 5 ml (0.02 mol) of phosphorous oxychloride under the reflux with stirring at 80ºC for 1 h. Further *see Method A*.

Oxadiazoles 9a-d obtained according to the Method A and Method B have the identical spectra, and their mixture does not give depression of melting points.

2-[(1S,3R),(1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]-5-phenyl-1,3,4-oxadiazole 9a. The yield is 86% (A), 71% (B). M.p. 110-111°C. Found, %: C 60.24, H 5.99, N 8.38. $C_{17}H_{19}Cl_2N_2O$. Calculated, %: C 60.12, H 5.94, N 8.26. ^{1}H NMR, δ, ppm: 0.65s (3H, CH_3), 1.28s (3H, CH_3), 1.38s (3H, CH_3), 1.64-1.94m (2H, CH_2CH_2), 2.03-2.28m (1H, CH_2CH_2), 2.59-2.85m (2H, CH, CH_2CH_2), 6.31d (1H, $CHCl_2$, J=9.1 Hz), 7.52-7.64m (3H, H-3,4,5), 7.94-8.02m (2H, H-2,6).

2-(2-Bromophenyl)-5-[(1S,3R),(1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]-1,3,4-oxadiazole 9b. The yield is 87% (A), 66% (B). M.p. 219-120°C. Found, %: C 48.73, H 4.49, N 6.88. $C_{17}H_{19}BrCl_2N_2O$. Calculated, %: C 48.83, H 4.58, N 6.70. ^{1}H NMR, δ, ppm: 0.82s (3H, CH_3), 1.09s (3H, CH_3), 1.20s (3H, CH_3), 1.30-1.47m (1H, CH_2CH_2), 1.56-1.80m (1H, CH_2CH_2), 1.87-2.10m (1H, CH_2CH_2), 2.23-2.56m (2H, CH, CH_2CH_2), 6,26d (1H, $CHCl_2$, J=8.8 Hz), 7.34-7.53m (3H, H-3,4,5), 7.66d (1H, H-6, J=7.0 Hz).

2-[(1S,3R),(1R,3S)*-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]-5-(3-nitrophenyl)-1,3,4-oxadiazole* 9c. The yield is 80% (A), 61% (B). M.p. 107-108°C. Found, %: C 53.18, H 4.91, N 11.02. $C_{17}H_{19}Cl_2N_3O_3$. Calculated, %: C 53.14, H 4.98, N 10.94. ^{1}H NMR, δ, ppm: 0.68s (3H, CH_3), 1.29s (3H, CH_3), 1.41s (3H, CH_3), 1.67-1.95m (2H, CH_2CH_2), 2.09-2.28m (1H, CH_2CH_2), 2.60-2.87m (2H, CH, CH_2CH_2), 6,32d (1H, $CHCl_2$, J=8.8 Hz), 7,88t (1H, H-5, J=7.7 Hz), 8.38-8.47m (2H, H-3,6), 8.64s (1H, H-2).

2-[(1S,3R),(1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]-5-(4-methoxyphenyl)-1,3,4-oxadiazole 9d. The yield is 84% (A), 68% (B). M.p. 101-102°C. Found, %: C 58.49, H 6.05, N 7.72. $C_{18}H_{22}Cl_2N_2O_2$. Calculated, %: C 58.54, H 6.00, N 7.59. ^{1}H NMR, δ, ppm: 0.65s (3H, CH_3), 1.27s (3H, CH_3), 1.37s (3H, CH_3), 1.63-1.92m (2H, CH_2CH_2), 2.05-2.28m (1H, CH_2CH_2), 2.55-2.85m (2H, CH, CH_2CH_2), 3.82s (3H, CH_3O), 6.31d (1H, $CHCl_2$, J=8.9 Hz), 7.12d (2H, H-3,5, J=8.6 Hz), 7.90d (2H, H-2,6, J=8.6 Hz).

Conclusions

To obtain new biologically active compounds the synthesis of intermediates – N'-aroylhydrazides of (±)-camphoric and (±)-cys-3-dichloromethyl-1,2,2-trimethylcyclopentancarboxylic acids have been done, and their different behaviour in dehydration reaction have been studied. As a result, it was shown that N'-aroylhydrazides of (±)-camphoric acid was not able to produce 1,3,4-oxadiazole derivatives being treated with dehydrating reagents. Therefore, another starting compound was suggested for the synthesis of 1,3,4-oxadiazoles with 1,2,2-trimethylcyclopentan moiety, namely, (±)-cis-3-dichloromethyl-1,2,2-trimethylcyclopentancarboxylic acid. Based on the latter the effective methods of synthesis of the target compounds were developed (61-71% yields). The structures of the compounds obtained were proved by methods of ^{1}H NMR spectroscopy and elemental analysis; purity was confirmed using thin layer chromatography. Also some specific characteristics of the signals splitting in the ^{1}H NMR spectra were revealed which might be used as analytical for camphoric acid derivatives.

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