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3-(PROP-2-YNYL)DIHYDROFURAN-2(3H)-ONES: SYNTHONES FOR LACTONE-CONTAINING NEW COMPOUNDS

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The behavior of 5,5-disubstituted-3-(prop-2-ynyl)dihydrofuran-2(3H)-ones under conditions of Mannich and coupling reactions have been studied. It was established that their interaction with paraform and secondary amines in the presence of copper halogenides (I) afforded aminobutynyl derivatives of γ-lactones, and the coupling reactions with active halogenides resulted in butynalkynyl derivatives. Synthesized compounds are representatives of new systems earlier not described in the literature.

***Keywords*:** propargyl lactones, secondary amines, bis-systems.

Introduction. It is known that a butanolide ring is a building block of various molecules of natural origin for both animal and plant world and a keen interest in lactone-containing compounds is explained by their high biological activity. Many widely used drugs: Pilocarpine, Spironolactone, Podofilox, Drospirenone, etc. as active ingredients contain compounds, in which a butanolide cycle is a constituent.

Despite more than a century history of chemistry of lactones, carries out intense researches into isolating compounds containing a butanolide fragment from natural sources and identifying their structures are still in progress. Methods for producing new butanolide derivatives are being developed along with the research to detect useful properties of lactone-containing compounds. Recent studies have shown that many isolated from various natural sources mono-, di- and sesquiterpenoids containing a butanolide moiety have a wide spectrum of biological activity. In particular, monoterpene glycoside isolated from the overground part of *Sibiraea angustata* RCHD has the effect of weight loss [1]. Penicillactone from marine fungus *Penicillinum sp.* PSU-F44 exhibits a stable antimicrobial effect against *Staphylococcus aureus* [2], sesquiterpene lactone *Zawadckiinolid F* inhibits LPS [3] and *Paramignyosides A-E* isolated from *Paramignya scandens* has a pronounced anti-inflammatory effect [4], etc.

Considering a promising potentiality of lactone-containing compounds, intensive research to develop new methods for producing compounds of this class has been carried out in recent years. Specifically, the method for obtaining spirooxindole butanolides [5], the method for the stereoselective synthesis of β-aminobutanolides [6], for condensing with aromatic cycle butanolides [7], etc.

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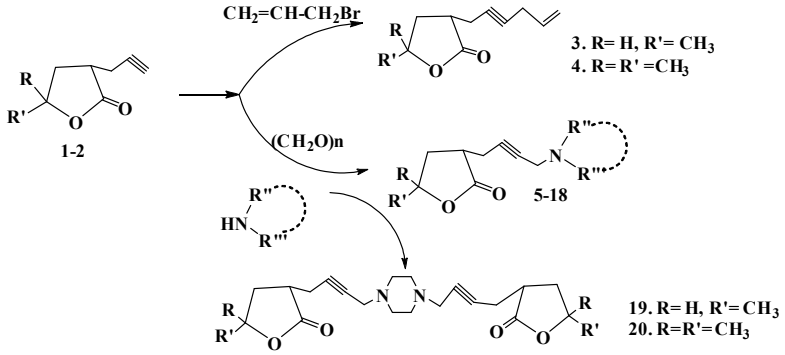
have been developed. Methods for producing functionally substituted butanolides become of great importance since they enable to synthesize their basis compounds of new classes containing a butanolide moiety. The examples include compounds with disubstituted alkinyl group [8], or those of natural products such as Nematin, which is allenbutadiyne butanolide derivative substituted in the 4th position [9].

It is evident that the research in the field of γ-lactones is reasonable and topical and the expected compounds can be of practical interest in pharmacology and medicine.

Materials and Methods. Earlier we had developed a number of methods for producing functionally substituted butanolides and synthesized based thereon heterocyclic compounds that demonstrated antibacterial and anti-inflammatory activities [10–12]. To continue these studies and aimed to extend the range of butanolide derivatives, examining the behavior of butanolides in different conditions, we have chosen 5,5-disubstituted-3-(prop-2-ynyl)dihydrofuran-2(3H)--ones (**1, 2**) as starting compounds (see Scheme). The presence of the terminal triple bond in the starting molecule will make it possible to deepen our knowledge in the field of γ-lactones, to pass to new classes of lactone-containing compounds. With this end in view, we have carried out research according to the Scheme:



5. R= H, R' = CH_3, R" = R"' = -$(CH_2)_2O(CH_2)_2$; 6. R=R'=CH_3, R" =R"' = -$(CH_2)_2O(CH_2)_2$; 7. R= H, R' = CH_3, R" =R"' = -C_2H_5; 8. R= R' = CH_3, R" =R"'= - C_2H_5; 9. R= H, R' = CH_3, R" =R"' = - $(CH_2)_5$; 10. R= R' = CH_3, R" =R"' = - $(CH_2)_5$; 11. R= H, R' = CH_3, R" =R"' = - $(CH_2)_5$; 12. R= R' = CH_3, R" =R"' = - $(CH_2)_5$; 13. R= H, R' = CH_3, R" = C_2H_5, R"' = - C_6H_5; 14. R= R' = CH_3, R" = C_2H_5, R"' = - C_6H_5; 15. R= H, R' = CH_3, R" =R"' = -C_4H_9; 16. R= R' = CH_3, R" =R"' = - C_4H_9; 17. R= H, R' = CH_3, R" =R"' = -$(CH_2CH_2)_2N(CH_3)$; 18. R= R' = CH_3, R" =R"' = -$(CH_2CH_2)_2N(CH_3)$.

To solve the assigned task, the behavior of **1**, **2** under conditions of coupling reaction with active halogenides has been studied. In particular, it was shown that in the atmosphere of inert gases (nitrogen, helium) dihydrofuranones **1**, **2** successfully coupled with allylbromide forming 2-(hex-5-en-2-ynyl)-5,5-disubstituted dihydrofuran-2(3H)-ones (**3**, **4**). Optimal conditions providing high yields of target products were found. It is shown that it is reasonable to carry out the reaction in the presence of potassium carbonate and copper chloride (I) in DMF.

Derivatives of secondary amines of various structures are known to be active aglycones of widely used drugs, such as Azafen, Fluacizine, Reksetin, Trazodone, Meklozin, Cinnarizine, etc. [13]. To introduce the mentioned pharmacophore groups into the structure of target products and to enlarge the range of lactone-containing compounds, the behavior of **1**, **2** under conditions of Mannich reaction have been studied. It is established that the interaction of starting reagents in the presence of catalytic CuCl resulted in formation of 5,5-disubstituted-3-(4-aminobut--2-ynyl)dihydrofuran-2(3H)-ones (**5**–**18**).

Thus, based on 5,5-disubstituted-3-(prop-2-ynyl)dihydrofuran-2(3H)-ones a method earlier not described in the literature for producing butanolide derivatives that can be of practical interest has been proposed.

Synthesized compounds have been characterized by physicochemical constants and analytical data, and their structures have been confirmed by NMR ^1H and ^{13}C data. The purity was controlled by TLC.

Experimental Part. ^1H and ^{13}C NMR spectra were registered on spectrometer Varian Mercury-300 from solution in DMSO : CCl_4=1: 3 or on Bruker AVANCE 400 *MHz* spectrometer in $CDCl_3$. Chemical shifts (δ) in *ppm* are reported as quoted relative to the residual signals of chloroform-*d* (7.25 for ^1H NMR and 77.0 for ^{13}C NMR) or DMSO-d_6 (2.49 for ^1H NMR and 39.5 for ^{13}C NMR) as internal references. The purity of obtained compounds was checked by TLC on Silufol UV-254 plates (development in iodine vapor). Melting points were determined on Boetius microheating stage.

Methods of synthesis of starting compounds **1**, **2** were described in [8].

General Procedure of Compounds 3, 4. On a mixture of 0.01 *mol* of corresponding 2-(propyn-2-yl)-4,4-disubstituted butanolide (**1, 2**), 0.015 *mol* allylbromide in the 10 *mL* abs. acetonitrile, 0.02 *mol* of potassium carbonate and 0.0015 *mol* CuCl were added, stirred 1 *h* at room temperature and 5 *h* at 50–60°*C*. The mixture was cooled and acidified to pH 4–5, extracted with diethyl ether and dried on $MgSO_4$. After distilling off the solvent, the residue was distilled under vacuum.

3-(Hex-5-en-2-ynyl)-5-methyldihydrofuran-2(3H)-one (3). Yield 70%, bp 119°*C*/2 *mm* Hg, R_f 0.50 (C_2H_5OH:C_6H_6=2:5), n_D^{20} 1.4765. Found, %: C 74.05; H 8.00. $C_{11}H_{14}O_2$. Calculated, %: C 74.13; H 7.92.

^1H NMR (300 *MHz*) spectrum, δ, *ppm*: 1.38 s (3H, CH_3); 1.98 t (1H, *J*=12.30 *Hz*, CH_2 in cycle); 2.26 dd (1H, *J*=12.7; 9.5 *Hz*, CH_2 in cycle); 2.47–2.56 m (2H, CH_2, $CH_2C{\equiv}C$); 2.81–3.32 m (3H,CH_2, CHO); 4.41 m (1H, CHO); 5.07 dq (1H, *J*=10.3; 1.6 *Hz*, CH=$\underline{CH_2}$); 5.26 dq (1H, *J*=17.5; 1.6 *Hz*, CH=$\underline{CH_2}$); 5.64–5.89 m (1H, $\underline{CH}$=CH_2).

3-(Hex-5-en-2-ynyl)-5,5-dimethyldihydrofuran-2(3H)-one (4). Yield 73%, bp 123–124°*C*/2 *mm* Hg, R_f 0.52 (C_2H_5OH:C_6H_6=2:5), n_D^{20} 1.4778. Found, %: C 74.90; H 8.20. $C_{12}H_{16}O_2$. Calculated, %: C 74.97; H 8.39.

^1H NMR (300 *MHz*) spectrum, δ, *ppm*: 1.39 s (3H, CH_3); 1.45 s (3H, CH_3); 1.99 t (1H, *J*=12.3 *Hz*, CH_2 in cycle); 2.27 dd (1 H, *J*=12.7; 9.5 *Hz*, CH_2 in cycle); 2.46–2.55 m (2H, $CH_2C{\equiv}C$); 2.83–3.02 m (3H, CHCO, CH_2); 5.07 dq (1H, *J*=10.3; 1.6 *Hz*, CH=$\underline{CH_2}$); 5.26 dq (1H, *J*=17.4; 1.5 *Hz*, CH=$\underline{CH_2}$); 5.63–5.89 m (1H, CH=$\underline{CH_2}$).

General Procedure of Aminmethylation Reaction. Compounds 5–20. A round bottom flask was placed 0.015 *mol* of the corresponding 2-(propyn-2-yl)--4,4-disubstituted butanolides, 0.0158 *mol* of secondary amine, 30 *mL* abs. dioxane, 1.55 *g* paraformaldehyde and 0.0015 *mol of* CuCl (I). The reaction mixture was heated to 100°*C*, for 8 *h*. The resulting solution was acidified to pH 3–4 and extracted with diethylether. After removing the solvent the residue was distilled under vacuum. For compounds **19–20** we used corresponding compounds with 0.0079 *mol* of secondary amine.

5-Methyl-3-(4-morpholinobut-2-ynyl)dihudrofuran-2(3H)-one (5). Yield 75%, bp 161°*C*/3 *mm* Hg, R_f 0.52 (C_2H_5OH : C_6H_6 : C_6H_{14} = 2 : 5 : 0.5); n_D^{20} 1.4990; d_4^{20} 1.1070. Found, %: C 65.90; H 8.10; N 6.00. $C_{13}H_{19}NO_3$ Calculated, %: C 65.80; H 8.07; N 5.90.

^{1}H NMR (300 *MHz*) spectrum, *δ*, *ppm*: 1.36 d (1H, *J*=6.4 *Hz*, CH_3); 1.40 d (2H, *J*=5.6 *Hz*, CH_3); 1.64–1.83 m (0.65H, CH_2 in cycle); 1.99–2.16 m (0.35H, CH_2 in cycle); 2.23–2.37 m (0.35H, CH_2 in cycle); 2.38–2.45 m (4H, CH_2N); 2.49–2.50 m (0.65H, CH_2 in cycle); 2.51–2.56 m (2H, $CH_2C{\equiv}C$); 2.79–2.94 m (1H, CHO); 3.19 s (2H, CH_2N); 3.53–3.67 m (4H, CH_2O); 4.42–4.59 m (0.65H, CHO); 4.62–4.74 m (0.35 H, CHO):

^{13}C NMR (300 *MHz*) spectrum, *δ*, *ppm*: 18.9; 19.5; 20.4; 20.9; 33.2; 35.0; 37.7; 39.9; 46.7 51.4; 73.8; 76.3; 81.2; 95.5; 104.8; 175.6; 175.9 (oxalate mp. 99ºC).

*5,5-Dimethyl-3-(4-morpholinobut-2-ynyl)dihudrofuran-2(3H)-one (**6**)*. Yield 70%, bp 161ºC/1 *mm* Hg, R_f 0.55 (C_2H_5OH: C_6H_6 : C_6H_{14} = 2 : 5 : 0.5), n_D^{20} 1.5000, d_4^{20} 1.1060. Found, %: C 66.90; H 8.40; N 5.60. $C_{14}H_{21}NO_3$. Calculated, %: C 66.91; H 8.42; N 5.57.

^{1}H NMR (300 *MHz*) spectrum, *δ*, *ppm*: 1.39 s (3H, CH_3); 1.47 s (3H, CH_3); 2.01 t (1H, *J*=11.9 *Hz*, CH_2 in cycle); 2.28 dd (1H, *J*=12.7; 9.5 *Hz*, CH_2 in cycle); 2.39–2.46 m (4H, CH_2N); 2.55 s (2H, $CH_2C{\equiv}C$); 2.94–3.06 m (1H, CHO); 3.19 s (2H, CH_2N); 3.55–3.63 m (4H, CH_2O).

^{13}C NMR (300 *MHz*) spectrum, *δ*, *ppm*: 19.1; 26.8; 28.3; 38.9; 39.2; 39.5; 39.8; 46.7; 51.4; 65.8; 76.4; 80.9; 81.2; 95.5; 174.9 (oxalate mp. 101–102ºC).

*3-(4-(Diethylamino)but-2-ynyl)-5-methyldihydrofuran-2(3H)-one (**7**).* Yield 65%; bp 143ºC/2 *mm* Hg, R_f 0.44 (C_2H_5OH : C_6H_6 : C_6H_{14} = 2 : 5 : 0.5); n_D^{20} 1.4770; d_4^{20}0.9951. Found, %: C 69.90; H 9.40; N 6.30. $C_{13}H_{21}NO_2$. Calculated, %: C 69.92; H 9.48; N 6.27.

^{1}H NMR (300 *MHz*) spectrum, *δ*, *ppm*: 1.01 t (5H, *J*=7.1 *Hz*, CH_2CH_3); 1.30 m (3H, CH_3); 2.00 m (1H, CH_2 in cycle); 2.23 m (1H, CH_2 in cycle); 2.43 q (4H, *J*=7.1 Hz, $\underline{CH_2}CH_3$); 2.50–2.55 m (2H, $CH_2C{\equiv}C$); 2.97 m (1H, CH=O); 3.30 s (2H, CH_2N); 4.42–4.59 m (0.65H, CHO); 4.62–4.74 m (0.35H, CHO).

^{13}C NMR (300 *MHz*) spectrum, *δ*, *ppm*: 12.2; 19.1; 26.7; 28.3; 39.1; 39.4; 39.5; 39.8; 39.9; 46.36; 76.2; 80.3; 80.8; 95.7; 174.9.

*3-(4-(Diethylamino)but-2-ynyl)-5,5-dimethyldihydrofuran-2(3H)-one (**8**)*. Yield 70%; bp 161ºC/2 *mm* Hg, R_f 0.51 (C_2H_5OH : C_6H_6 : C_6H_{14}=2 : 5 : 0.5); n_D^{20} 1.4900; d_4^{20} 0.9784. Found, %: C 70.80; H 9.73; N 5.92. $C_{14}H_{23}NO_2$. Calculated, %: C 70.85; H 9.77; N 5.90.

^{1}H NMR (300 *MHz*) spectrum, *δ*, *ppm*: 1.01 t (6H, *J*=7.1 *Hz*, $CH_2\underline{CH_3}$); 1.37–1.47 m (6H, CH_3); 2.00 m (1H, CH_2 in cycle); 2.23 m (1H, CH_2 in cycle); 2.43 q (4H, *J*=7.1 *Hz*, $\underline{CH_2}CH_3$); 2.50–2.55 m (2H, $CH_2C{\equiv}C$); 2.97 m (1H, CHCO); 3.30 s (2H, CH_2N).

^{13}C NMR (75 *MHz*) spectrum, *δ*, *ppm*: 12.2; 19.1; 26.7; 28.3; 39.1; 39.4; 39.5; 39.8; 39.9; 46.36; 76.2; 80.3; 95.7; 174.9.

*5-Methyl-3-(4-(piperidin-1-yl)but-2-ynyl)dihydrofuran-2(3H)-one (**9**)*. Yield 70%; bp 145ºC/2 *mm* Hg, R_f 0.56 (C_2H_5OH : C_6H_6 : C_6H_{14}=2 : 5 : 0.5); n_D^{20} 1.4900; d_4^{20}1.0210. Found, %: C 71.42; H 8.73; N 5.95. $C_{14}H_{21}NO_2$. Calculated, %: C 71.46; H 8.99; N 5.95.

^{1}H NMR (400 *MHz*) spectrum, *δ*, *ppm*: 1.32–1.44 m (5H, CH_2,CH_3); 1.51–1.61 m (4H, CH_2); 1.94–2.05 m (1H, CH_2 in furanone); 2.26 m (1H, CH_2 in furanone); 2.40 br.s. (4H, CH_2N); 2.48–2.56 m (1H, $CH_2C{\equiv}C$); 2.58–2.68 m (1H, $CH_2C{\equiv}C$); 2.86–2.97 m (1H, CHO); 3.17 m (2H, CH_2N); 4.40 m (1H, CHO).

^{13}C NMR (101 *MHz*) spectrum, *δ*, *ppm*: 19.5; 23.4; 26.9; 28.4; 39.8; 47.7; 52.9; 77.3; 80.4; 176.4 (oxalate mp. 120ºC).

5,5-Dimethyl-3-(4-(piperidin-1-yl)but-2-ynyl)dihydrofuran-2(3H)-one ***(10)***. Yield 78%; bp 155°*C*/2 *mm* Hg, R_f 0.55 (C_2H_5OH : C_6H_6 : C_6H_{14} = 2 : 5 : 0.5); n_D^{20} 1.4930; d_4^{20}1.0269. Found, %: C 72.20; H 9.23, N 5.65. $C_{15}H_{23}NO_2$. Calculated, %: C 72.25; H 9.30; N 5.62.

^{1}H NMR (400 *MHz*) spectrum, *δ*, *ppm*: 1.32–1.42 m (5H, CH_2,CH_3); 1.44 d (3H, *J*=3.9 *Hz*, CH_3); 1.51–1.62 m (4H, CH_2); 1.95–2.07 m (1H; CH_2 in furanone); 2.26 m (1H, CH_2 in furanone); 2.41 br. s. (4H, CH_2N); 2.48–2.56 m (1H, $CH_2C{\equiv}C$); 2.58–2.68 m (1H, $CH_2C{\equiv}C$); 2.86–2.97 m (1H, CHC=O); 3.17 m (2H, CH_2N).

^{13}C NMR (101 *MHz*) spectrum, *δ*, *ppm*: 19.6; 23.4; 25.4; 26.8; 28.4; 39.8; 47.5; 52.9; 77.3; 80.4; 82.4; 176.4 (oxalate mp. 142–143°*C*).

5-Methyl-3-(4-(pyrrolidin-1-yl)but-2-ynyl)dihydrofuran-2(3H)-one ***(11)***. Yield 75%; bp 138°*C*/2 *mm* Hg, R_f 0.47 (C_2H_5OH : C_6H_6 : C_6H_{14} = 2 : 5 : 0.5); n_D^{20} 1.4850; d_4^{20}1.0300. Found, %: C 70.42; H 8.53; N 6.55. $C_{13}H_{19}NO_2$. Calculated, %: C 70.56; H 8.65; N 6.33.

^{1}H NMR (400 *MHz*) spectrum, *δ*, *ppm*: 1.33 d (3H, *J*=3.5 *Hz*, CH_3); 1.73 br.d (4H, *J*=3.3 *Hz*, CH_2 in pyrrolidin); 1.93–2.04 m (1H, CH_2 in furanone); 2.25 ddd (1H, *J*=12.6; 9.3; 3.5 *Hz*, CH_2 in furanone); 2.42–2.65 m (6H, CH_2N, $CH_2C{\equiv}C$); 2.91 qd (1H, *J*=7.8; 4.3 *Hz*, CHCO); 3.29 br.d (2 H, *J*=2.7 *Hz*, CH_2N); 4.45 m (1H, CHO).

^{13}C NMR (101 *MHz*) spectrum, *δ*, *ppm*: 23.4; 26.4; 28.0; 39.8; 42.5; 52.0; 77.3; 80.0; 81.9; 176.4.

5,5-Dimethyl-3-(4-(pyrrolidin-1-yl)but-2-ynyl)dihydrofuran-2(3H)-one ***(12)***. Yield 85%; bp 141°*C*/2 *mm* Hg, R_f 0.54 (C_2H_5OH : C_6H_6 : C_6H_{14} = 2 : 5: 0.5); n_D^{20} 1.4880; d_4^{20} 1.0338. Found, %: C 71.42; H 8.83; N 6.00. $C_{13}H_{19}NO_2$. Calculated, %: C 71.46; H 8.99; N 5.95.

^{1}H NMR (400 *MHz*) spectrum, *δ*, *ppm*: 1.33 d (3H, *J*=3.5 *Hz*, CH_3); 1.42 d (3H, *J*=3.9 *Hz*, CH_3); 1.73 br.d (4H, *J*=3.5 *Hz*, CH_2 in pyrrolidin); 1.93–2.04 m (1H, CH_2 in furanone); 2.25 ddd (1H, *J*=12.6; 9.3; 3.5 *Hz*, CH_2 in furanone); 2.42–2.65 m (6H, CH_2N, $CH_2C{\equiv}C$); 2.91 m (1H, CHO); 3.29 br.d (2H, *J*=2.7 *Hz*, CH_2N).

^{13}C NMR (101 *MHz*) spectrum, *δ*, *ppm*: 19.5; 23.3; 26.8; 28.3; 39.8; 42.8; 52.1; 77.7; 79.8; 82.0; 176.4.

3-(4-(Ethyl(phenyl)amino)but-2-ynyl)-5-methyldihydrofuran-2(3H)-one ***(13)***. Yield 70%; bp 184°*C*/2 *mm* Hg, R_f 0.59 (C_2H_5OH : C_6H_6 : C_6H_{14} = 2 : 5 : 0.5); n_D^{20} 1.5512; d_4^{20} 1.0855. Found, %: C 70.80; H 9.73; N 5.92. $C_{14}H_{23}NO_2$. Calculated, %: C 70.85; H 9.77; N 5.90.

^{1}H NMR (300 *MHz*) spectrum, *δ*, *ppm*: 1.19 t (3H, *J*=7.1 *Hz*, $\underline{CH_3}CH_2$); 1.27 d (3H, *J*=6.4 *Hz*, CH_3); 1.56–1.72 m (0.7H, CH_2 in furanone); 1.83–1.99 m (0.3H, CH_2 in furanone); 2.11–2.22 m (0.3H, CH_2 in furanone); 2.26–2.44 m (0.7H, CH_2 in furanone); 2.72–2.92 m (1H, CHCO); 3.41 q (2H, *J*=7.1 *Hz*, $CH_3\underline{CH_2}$); 3.99 s (2H, CH_2N); 4.34–4.54 m (1H, CHO); 6.56–6.81 m (3H, H_{arom}); 7.07–7.26 m (2H, H_{arom}).

^{13}C NMR (75 *MHz*) spectrum, *δ*, *ppm*: 11.9; 28.7; 39.0; 39.2; 39.5; 39.8; 40.6; 44.6; 73.8; 78.2; 79.4; 80.2; 95.5; 113.6; 116.6; 128.3; 147.3.

3-(4-(Ethyl(phenyl)amino)but-2-ynyl)-5,5-dimethyldihydrofuran-2(3H)-one ***(14)***. Yield 70%; bp 175°*C*/1 *mm* Hg, R_f 0.64 (C_2H_5OH : C_6H_6 : C_6H_{14} = 2 : 5 : 0.5); n_D^{20} 1.5530; d_4^{20} 1.0865. Found, %: C 75.70; H 8.03; N 5.00. $C_{18}H_{23}NO_2$. Calculated, %: C 75.76; H 8.12; N 4.91.

^{1}H NMR (300 *MHz*) spectrum, *δ*, *ppm*: 1.19 t (3H, *J*=7.1 *Hz*, $\underline{CH_3}CH_2$); 1.21 d (3H, *J*=6.4 *Hz*, CH_3); 1.27 d (3H, *J*=6.4 *Hz*, CH_3); 1.56–1.72 m (0.7H, CH_2 in furanone); 1.83–1.99 m (0.3H, CH_2 in furanone); 2.10–2.20 m (0.3H, CH_2 in furanone);

2.26–2.44 m (0.7H, CH_2 in furanone); 2.72–2.90 m (1H, CHCO); 3.41 q (2H, *J*=7.1 *Hz*, $\underline{CH_2}CH_3$); 3.99 s (2H, CH_2N); 6.56–6.81 m (3H, H_{arom}); 7.07–7.26 m (2H, H_{arom}).

^{13}C NMR (75 *MHz*) spectrum, *δ*, *ppm*: 11.9; 28.7; 39.0; 39.2; 39.5; 39.8; 40.6; 44.6; 73.8; 78.2; 79.4; 80.2; 95.5; 113.6; 116.6; 128.3; 147.3.

*3-(4-(Dibutylamino)but-2-ynyl)-5-methyldihydrofuran-2(3H)-one (**15**).* Yield 65%; bp 115°*C*/2 *mm* Hg, R_f 0.40 (C_2H_5OH : C_6H_6 : C_6H_{14} = 2 : 5 : 0.5); n_D^{20} 1.4740; d_4^{20} 0.9574. Found, %: C 75.70; H 8.03; N 5.00. $C_{17}H_{29}NO_2$. Calculated, %: C 73.07; H 10.46; N 5.01.

^1H NMR (300 *MHz*) spectrum, *δ*, *ppm*: 0.86–0.98 m (6H, CH_3); 1.21–1.53 m (11H, in Bu, CH_3); 1.93–2.07 m (1H, CH_2 in furanone); 2.07–2.31 m (1H, CH_2 in furanone); 2.31–2.40 m (4H, CH_2N); 2.53 dt (2H, *J* = 5.6; 2.1 *Hz*, $CH_2C{\equiv}C$); 2.84– 3.07 m (1H, CHCO); 3.27 t (2H, *J*=2.1 *Hz*, CH_2N); 4.51 m (1H, CHO).

^{13}C NMR (75 *MHz*, DMSO) spectrum, *δ*, *ppm*: 13.5; 26.7; 28.3; 29.1; 32.6; 39.1; 39.3; 39.5; 39.8; 41.1; 52.5; 76.5; 80.4; 80.7; 174.8.

*3-(4-(Dibutylamino)but-2-ynyl)-5,5-dimethyldihydrofuran-2(3H)-one (**16**).* Yield 65%; bp 163°*C*/2 *mm* Hg, R_f 0.44 (C_2H_5OH : C_6H_6 : C_6H_{14} = 2 : 5 : 0.5); n_D^{20} 1.4724; d_4^{20} 0.9543. Found, %: C 73.70; H 10.60; N 5.00. $C_{18}H_{31}NO_2$. Calculated, %: C 73.67; H 10.65; N 4.77.

^1H NMR (300 *MHz*) spectrum, *δ*, *ppm*: 0.86–0.98 m (6H, CH_3 in Bu); 1.22–1.55 m (14H, CH_2 in Bu, CH_3); 1.93–2.07 m (1H, CH_2 in furanone); 2.07–2.31 m (1H, CH_2 in furanone); 2.30–2.39 m (4H, CH_2N); 2.53 dt (2H, *J* = 5.6; 2.1 *Hz*, $CH_2C{\equiv}C$); 2.85–3.05 m (1H, CHCO); 3.27 t (2H, *J* = 2.1 *Hz*, CH_2N).

^{13}C NMR (75 *MHz*) spectrum, *δ*, *ppm*: 13.7; 19.1; 19.8; 26.8; 28.3; 29.0; 32.1; 38.9; 39.1; 39.4; 39.7; 40.0; 52.7; 77.0; 80.5; 81.0; 173.8.

*5-Methyl-3-(4-(4-methylpiperazin)-1-yl)but-2-ynyl)dihydrofuran-2(3H)-one (**17**).* Yield 60%; bp 174°*C*/2 *mm* Hg, R_f 0.58 (C_2H_5OH : C_6H_6 : C_6H_{14} = 2 : 5 : 0.5); n_D^{20} 1.5000; d_4^{20}1.0547. Found, %: C 67.02; H 8.53; N 11.25. $C_{14}H_{22}N_2O_2$. Calculated, %: C 67.17; H 8.86; N 11.19.

^1H NMR (400 *MHz*) spectrum, *δ*, *ppm*: 1.31 dd (1H, *J* = 6.4; 0.7 *Hz*, CH_3); 1.36 dd (2H, *J* = 6.1; 0.6 *Hz*, CH_3); 1.72 dd (0.65H, *J* = 22.8; 11.9 *Hz*, CH_2 in furanone); 1.95–2.09 m (0.35H, CH_2 in furanone); 2.20 s (3H, CH_3N); 2.29–2.67 m (10H, CH_2 in furanone, CH_2N, $CH_2C{\equiv}C$); 2.67–2.89 m (2H, $CH_2C{\equiv}C$, CHCO); 3.18 s (2H, CH_2N); 4.39–4.51 m (0.65H, CHO); 4.61–4.72 m (0.35H, CHO).

^{13}C NMR (101 *MHz*) spectrum, *δ*, *ppm*: 19.3; 19.9; 20.4; 20.8; 33.5; 35.5; 38.1; 40.4; 45.4; 46.6; 51.4; 54.4; 74.7; 74.9; 76.6; 80.7; 80.8; 176.7.

*5,5-Dimethyl-3-(4-(4-methylpiperazin)-1-yl)but-2-ynyl)dihydrofuran-2(3H)-one (**18**).* Yield 65%; bp 185°*C*/2 *mm* Hg, R_f 0.55 (C_2H_5OH : C_6H_6 : C_6H_{14} = 2 : 5 : 0.5); n_D^{20} 1.4962; d_4^{20}1.0429. Found, %: C 67.02; H 8.53; N 11.25. $C_{15}H_{24}N_2O_2$. Calculated, %: C 68.15; H 9.15; N 10.60.

^1H NMR (400 *MHz*) spectrum, *δ*, *ppm*: 1.30 d (3H, *J*=3.5 *Hz*, CH_3); 1.41 d (3H, *J* = 3.5 *Hz*, CH_3); 1.96–2.09 m (1H, CH_2 in furanone); 2.21 s (3H, CH_3N); 2.30–2.67 m (10H, CH_2N, CH_2 in furanone, $CH_2C{\equiv}C$); 2.67–2.88 m (2H, $CH_2C{\equiv}C$, CHCO); 3.18 s (2H, CH_2N).

^{13}C NMR (101 *MHz*) spectrum, *δ*, *ppm*: 19.3; 19.9; 20.4; 20.8; 33.5; 35.5; 38.1; 40.4; 45.4; 46.6; 51.4; 54.4; 74.7; 74.9; 76.6; 80.7; 80.8; 176.7.

*3,3'-(4,4'-piperazin-1,4-diyl)bis(but-2-yn-4,1-diyl)bis(5-methyldihydrofuran)-2(3H)one (**19**).* Yield 70%; mp 120°*C* (diethyl ether), R_f 0.50 (C_2H_5OH : C_6H_6 : C_6H_{14}

=2 :5:0.5). Found, %: C 68.30; H 7.53; N 7.52. $C_{22}H_{30}N_2O_4$. Calculated, %: C 68.37; H 7.82; N 7.25.

^{1}H NMR (400 *MHz*) spectrum, *δ*, *ppm*: 1.35 d (1.5H, *J* = 6.4 *Hz*, CH_3); 1.41 d (4.5H, *J* = 6.1 *Hz*, CH_3); 1.76 dt (1.5H, *J* = 23.0; 11.5 *Hz*, CH_2 in furanone); 2.06 ddd (0.5H, *J* = 13.4; 9.3; 4.3 *Hz*, CH_2 in furanone); 2.15 s (1H, CH_2 in furanone); 2.34 dt (0.5H, *J* = 12.9; 7.9 *Hz*, CH_2 in furanone); 2.41–2.70 m (12.5 H, CH_2 in furanone, $CH_2C{\equiv}C$, CH_2N); 2.71–2.91 m (2H, CHCO); 3.23 s (4H, CH_2N); 4.39–4.58 m (1.5H, CHO); 4.70 dd (0.5H, *J* = 11.4; 6.8 *Hz*, CHO).

^{13}C NMR (101 *MHz*) spectrum, *δ*, *ppm*: 19.3; 19.9; 20.4; 20.6; 33.6; 35.5; 38.2; 40.4; 46.6; 51.3; 74.7; 74.8; 80.7; 80.9; 109.5; 176.7.

*3,3'-(4,4'-piperazin-1,4-diyl)bis(but-2-yn-4,1-diyl)bis(5,5-dimethyldihydrofuran)--2(3H)one (**20**)*. Yield 75%; mp 129ºC (diethyl ether), R_f 0.53 (C_2H_5OH : C_6H_6: C_6H_{14}= =2:5:0.5. Found, %: C 69.30; H 8.13; N 6.92. $C_{24}H_{34}N_2O_4$. Calculated, %: C 69.56; H 8.21; N 6.76.

^{1}H NMR (400 *MHz*) spectrum, *δ*, *ppm*: 1.33 s (6H, CH_3); 1.42 s (6H, *J* = 13.0 *Hz*, CH_3); 1.96 t (2H, *J* = 12.1 *Hz*, CH_2 in furanone); 2.26 dd (2H, *J* = 12.5; 9.1 *Hz*, CH_2 in furanone); 2.43–2.71 m (10H, CH_2 in furanone, $CH_2C{\equiv}C$, CH_2N); 2.83–2.99 m (2H,CHCO); 3.24 s (4H, CH_2N); 3.34–3.93 m (2H, $CH_2C{\equiv}C$).

^{13}C NMR (101 *MHz*) spectrum, *δ*, *ppm*: 19.3; 19.9; 20.4; 20.6; 26.8; 28.8; 33.6; 35.5; 38.2; 40.4; 46.6; 51.3; 74.7; 74.8; 76.1; 80.7; 80.9; 81.5; 82.1; 109.5; 176.7.

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