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SYNTHESIS OF CYCLOPROPYL-SUBSTITUTED 4H-3,1-BENZOXAZINES FROM 2-AMINO-PHENYL CYCLOPROPYL KETONES AND 2-CYCLOPROPANOYLAMINOACYLBENZENES

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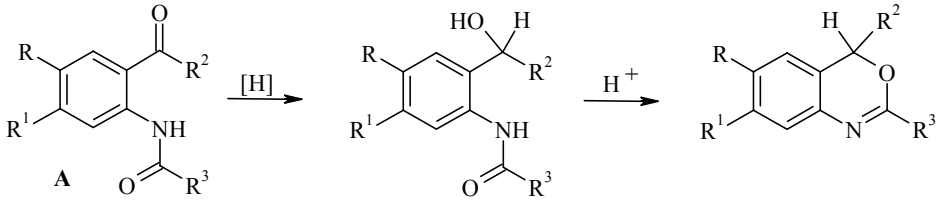
2- and 4-cyclopropyl- and 2,4-dicyclopropyl-substituted 4H-3,1-benzoxazines were synthesized by the intramolecular acid catalyzed heterocyclization of ortho-acylamino-substituted benzyl alcohols, obtained from 2-aminophenyl cyclopropyl ketones and 2-cyclopropanoylaminoacylbenzenes.

Keywords: 7-acyl-6-amino-1,4-benzodioxane, 4-amino-5-cyclopropanoylveratrole, 7-acyl-6-acylamino-1,4-benzodioxanes, 2-acylamino-4,5-dimethoxybenzyl alcohols, 4-acylamino-5-cyclopropanoylveratroles, 2-acylamino-4,5-ethylenedioxybenzyl alcohols, 6-cyclopropanoyl-1,4-benzodioxane, 4-cyclopropanoyl-veratrole, cyclopropyl-substituted 4H-3,1-benzoxazines, intramolecular heterocyclization.

4H-3,1-Benzoxazines occupy an important place in a series of heterocyclic compounds, among which there is an intensive search for new medicinal substances [1-3]. A series of effective methods of synthesis have been developed recently [4-8] by which, in principle, one can obtain a wide range of functionally-substituted 4H-3,1-benzoxazines – potential objects for testing for biological activity. Benzoxazines containing cyclopropane units are missing from the 4H-3,1-benzoxazines synthesized so far.

In our opinion, the reason why cyclopropyl-substituted benzoxazines have not been obtained so far is because of the high probability of modification of the three-carbon ring in the conditions for forming the heterocyclic 3,1-benzoxazine structure. Another factor repressing the synthesis of cyclopropyl-substituted benzoxazines is evidently the difficulty of preparing cyclopropane derivatives – the precursors of the required heterocycles.



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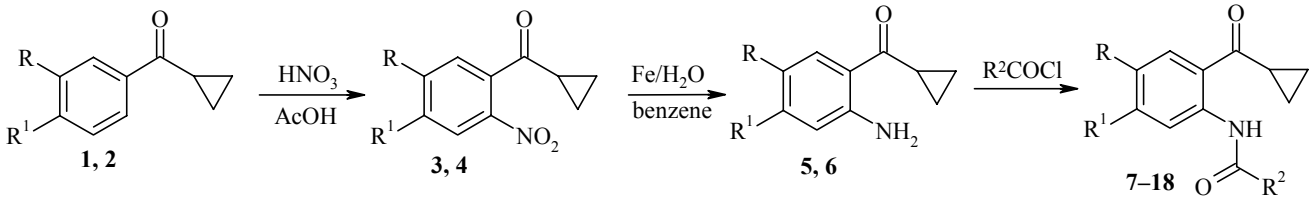
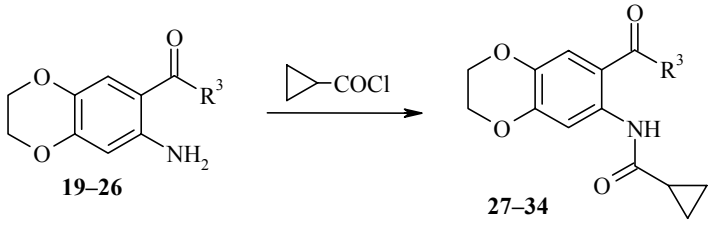
We have shown [8] that substituted 4H-3,1-benzoxazines are formed in high yields from 2-acylamino-acylbenzenes by successive reduction of the ketone function to the corresponding benzyl alcohols followed by cyclization of the latter under the influence of sulfuric or trifluoroacetic acid.

We proposed that similar successive conversions might be used for the synthesis of cyclopropyl-substituted 4H-3,1-benzoxazines from the corresponding predecessors. To confirm our idea we carried out the synthesis of cyclopropyl-substituted analogs of compounds of type **A** (R^2 or R^3 = cyclopropyl) and studied the possibility of converting them into cyclopropyl-substituted 4H-3,1-benzoxazines according to the methodology proposed previously [8].

The correspondingly 6-acylamino-7-cyclopropanoyl-1,4-benzodioxanes **7-12**, 4-acylamino-5-cyclopropanoylveratroles **13-18**, and also 6-acyl-7-cyclopropanoylaminobenzodioxanes **27-34** were obtained for the first time from cyclopropanoyl benzenes **1,2** and 7-acyl-6-amino-1,4-benzodioxanes **19-26**.



1, **3**, **5**, **7–12** R–R^1 = OCH_2CH_2O; **7** R^2 = cyclopropyl, **8** R^2 = 2-furyl, **9** R^2 = 2-thienyl, **10** R^2 = *o*-BrC_6H_4, **11** R^2 = *p*-FC_6H_4, **12** R^2 = *m*-FC_6H_4; **2**, **4**, **6**, **13–18** R = R^1 = OMe, **13** R^2 = cyclopropyl, **14** R^2 = 2-furyl, **15** R^2 = 2- thienyl, **16** R^2 = *o*-FC_6H_4; **17** R^2 = *p*-FC_6H_4, **18** R^2 = *p*-$MeOC_6H_4OCH_2$



19, **27** R^3 = Me; **20**, **28** R^3 = *i*-Pr; **21**, **29** R^3 = Ph; **22**, **30** R^3 = *p*-MeC_6H_4; **23**, **31** R^3 = *p*-BrC_6H_4; **24**, **32** R^3 = *o*-FC_6H_4; **25**, **33** R^3 = *m*-FC_6H_4; **26**, **34** R^3 = *p*-$MeOC_6H_4$

Reduction of the acylamino ketones **7-18**, **27-34** with $NaBH_4$ to the benzyl alcohols **35-46**, **58-65** with direct conversion to the corresponding cyclopropyl-substituted 4H-3,1-benzoxazines proceeded without complications in high yield (Table 1). However the high effectiveness of the reduction process was only achieved with a 1:1 ratio of substrate to $NaBH_4$, while a smaller ratio is normally used for the reduction aryl ketones. In all probability the steric hindrance caused by the *ortho* substituents, making reduction of the carbonyl difficult, results in the necessity of using equimolar quantities.

It should be noted that even in our conditions compound **18** was reduced with difficulty (it required a long time and heating) which is probably connected with the size of the substituent on the amide nitrogen, which affects the coordination of the reducing agent to the carbonyl group of the *ortho*-acyl substituent.

Table 1. Characteristics of Compounds **7-18**, **27-73**

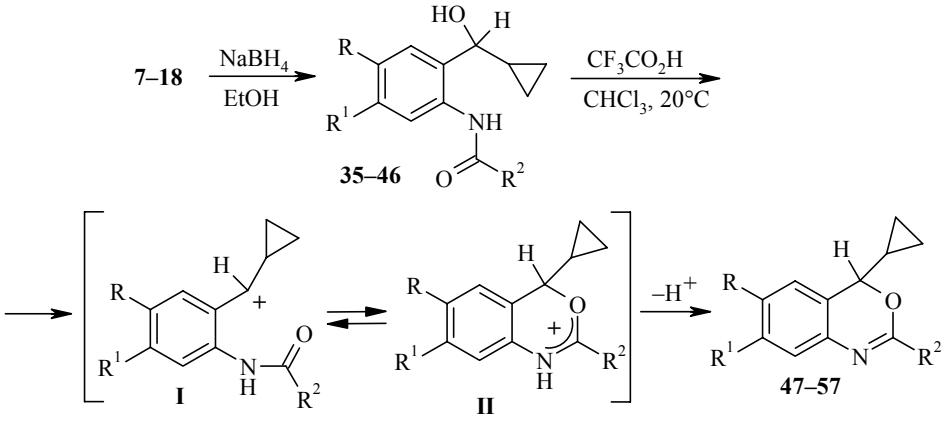
Compound	Empirical formula	Found, % / Calculated, %			mp, °C (solvent for crystallization)	Yield, %
		C	H	N		
1	2	3	4	5	6	7
7	$C_{16}H_{17}NO_4$	66.71 / 66.88	5.79 / 5.97	4.71 / 4.88	146-147 (ethanol)	83
8	$C_{17}H_{15}NO_5$	64.91 / 65.17	4.65 / 4.82	4.28 / 4.47	211-212 (ethanol–$CHCl_3$)	86
9	$C_{17}H_{15}NO_4S$	61.72 / 61.99	4.43 / 4.59	4.01 / 4.25	171-172 (ethanol)	91
10	$C_{19}H_{16}BrNO4$	56.51 / 56.73	3.82 / 4.01	3.56 / 3.48	215-216 (ethanol–$CHCl_3$)	89
11	$C_{19}H_{16}FNO_4$	66.56 / 66.85	4.54 / 4.73	4.14 / 4.10	230-231 (ethanol–$CHCl_3$)	87
12	$C_{19}H_{16}FNO_4$	66.64 / 66.85	4.51 / 4.73	3.96 / 4.10	158-159 (ethanol–$CHCl_3$)	79
13	$C_{16}H_{19}NO_4$	66.11 / 66.42	6.44 / 6.62	4.53 / 4.84	132-133 (ethanol)	81
14	$C_{17}H_{17}NO_5$	64.58 / 64.75	5.31 / 5.43	4.26 / 4.44	148-149 (ethanol)	84
15	$C_{17}H_{17}NO_4S$	61.41 / 61.62	5.01 / 5.17	4.03 / 4.23	146-147 (ethanol)	92
16	$C_{19}H_{18}FNO_4$	66.17 / 66.46	5.11 / 5.28	3.97 / 4.08	126-127 (ethanol)	88
17	$C_{19}H_{18}FNO_4$	66.22 / 66.46	5.08 / 5.28	3.92 / 4.08	168-169 (ethanol)	81
18	$C_{21}H_{23}NO_6$	65.16 / 65.44	5.88 / 6.01	3.71 / 3.63	137-138 (ethanol)	85
27	$C_{14}H_{15}NO_4$	64.11 / 64.36	5.65 / 5.79	5.12 / 5.36	169-170 (ethanol)	91
28	$C_{16}H_{19}NO_4$	66.21 / 66.42	6.43 / 6.62	4.61 / 4.84	120-121 (ethanol)	81
29	$C_{19}H_{17}NO_4$	70.28 / 70.57	5.11 / 5.30	4.42 / 4.33	152-153 (ethanol)	87
30	$C_{20}H_{19}NO_4$	70.92 / 71.20	5.44 / 5.68	3.98 / 4.15	153-154 (ethanol)	93
31	$C_{19}H_{16}BrNO_4$	56.41 / 56.73	3.82 / 4.01	3.21 / 3.42	171-172 (ethanol–$CHCl_3$)	92
32	$C_{19}H_{16}FNO_4$	66.58 / 66.85	4.52 / 4.73	4.02 / 4.10	141-142 (ethanol–$CHCl_3$)	84
33	$C_{19}H_{16}FNO_4$	66.68 / 66.85	4.54 / 4.73	3.92 / 4.10	182-183 (ethanol)	83
34	$C_{20}H_{19}NO_5$	67.71 / 67.98	5.18 / 5.42	3.73 / 3.96	111-112 (ethanol)	88
35	$C_{16}H_{19}NO_4$	66.01 / 66.42	6.31 / 6.62	4.91 / 4.84	119-120 (ethanol)	71
36	$C_{17}H_{17}NO_5$	64.45 / 64.75	5.21 / 5.43	4.32 / 4.44	152-153 (ethanol–water)	81
37	$C_{17}H_{17}NO_4S$	61.31 / 61.62	4.93 / 5.17	4.12 / 4.23	164-165 (ethanol–water)	84
38	$C_{19}H_{18}BrNO_4$	56.21 / 56.45	4.21 / 4.49	3.26 / 3.47	118-120 (ethanol)	74
39	$C_{19}H_{18}FNO_4$	66.21 / 66.46	5.04 / 5.28	3.82 / 4.08	168-169 (ethanol–water)	85
40	$C_{19}H_{18}FNO_4$	66.19 / 66.46	5.14 / 5.28	3.91 / 4.08	115-117 (ethanol)	76
41	$C_{16}H_{21}NO_4$	65.55 / 65.96	7.03 / 7.27	4.59 / 4.81	140-141 (ethanol)	78
42	$C_{17}H_{19}NO_5$	64.01 / 64.34	5.82 / 6.03	4.31 / 4.41	119-120 (ethanol)	87
43	$C_{17}H_{19}NO_4S$	60.88 / 61.24	5.52 / 5.74	3.99 / 4.20	126-127 (ethanol)	91
44	$C_{19}H_{20}FNO_4$	65.78 / 66.08	5.61 / 5.84	3.91 / 4.06	117-118 (ethanol)	81

Table 1 (continued)

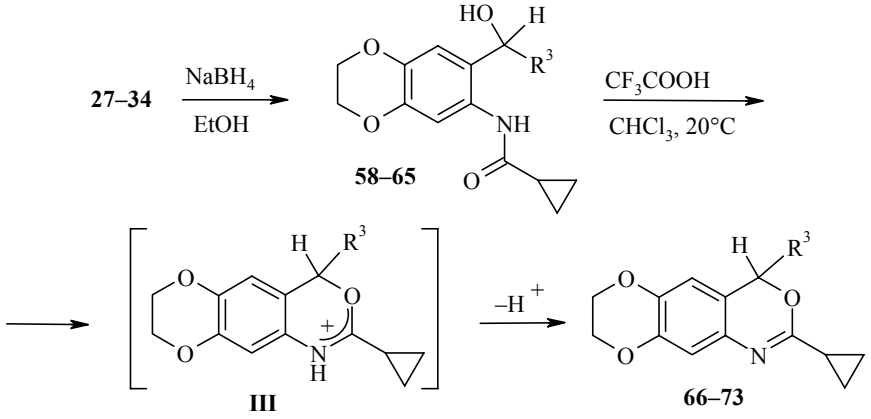
1	2	3	4	5	6	7
45	$C_{19}H_{20}FNO_4$	65.86 / 66.08	5.66 / 5.84	3.82 / 4.06	161-162 (ethanol–$CHCl_3$)	84
46	$C_{21}H_{25}NO_6$	64.81 / 65.10	6.27 / 6.50	3.41 / 3.62	—*	83
47	$C_{16}H_{17}NO_3$	70.44 / 70.83	6.12 / 6.32	4.94 / 5.16	—*	69
48	$C_{17}H_{15}NO_4$	68.39 / 68.67	4.92 / 5.09	4.48 / 4.71	—*	61
49	$C_{17}H_{15}NO_3S$	64.85 / 65.15	4.69 / 4.83	4.25 / 4.47	—*	90
50	$C_{19}H_{16}BrNO_3$	58.77 / 59.08	3.95 / 4.18	3.41 / 3.63	117-118 (ethanol)	78
51	$C_{19}H_{16}FNO_3$	70.35 / 70.14	4.85 / 4.96	4.27 / 4.31	131-132 (ethanol)	81
52	$C_{19}H_{16}FNO_3$	69.91 / 70.14	4.71 / 4.96	4.14 / 4.31	84-85 (ether)	76
53	$C_{16}H_{19}NO_3$	70.02 / 70.31	6.85 / 7.01	4.91 / 5.12	—*	75
54	$C_{17}H_{17}NO_4$	68.10 / 68.21	5.66 / 5.72	4.57 / 4.68	110-111 (ether)	77
55	$C_{17}H_{17}NO_3S$	64.58 / 64.74	5.22 / 5.43	4.26 / 4.44	—*	84
56	$C_{19}H_{18}FNO_3$	69.36 / 69.71	5.31 / 5.54	4.11 / 4.28	—*	74
57	$C_{19}H_{18}FNO_3$	68.94 / 69.71	5.53 / 5.54	4.08 / 4.28	115-116 (ether–petroleum ether)	85
58	$C_{14}H_{17}NO_4$	63.54 / 63.87	6.29 / 6.51	5.14 / 5.32	124-125 (ethanol)	77
59	$C_{16}H_{21}NO_4$	65.68 / 65.96	7.02 / 7.27	4.56 / 4.81	134-135 (ethanol)	82
60	$C_{19}H_{19}NO_4$	69.81 / 70.14	5.68 / 5.89	4.14 / 4.31	166-167 (ethanol)	79
61	$C_{20}H_{21}NO_4$	70.56 / 70.78	6.13 / 6.24	3.98 / 4.13	157-158 (ethanol)	74
62	$C_{19}H_{18}NBrO_4$	56.11 / 56.45	4.21 / 4.49	3.38 / 3.47	161-162 (ethanol)	81
63	$C_{19}H_{18}FNO_4$	66.14 / 66.46	5.19 / 5.28	3.92 / 4.08	167-168 (ethanol)	77
64	$C_{19}H_{18}FNO_4$	66.21 / 66.46	5.09 / 5.28	3.89 / 4.08	143-144 (ethanol–water)	84
65	$C_{20}H_{21}NO_5$	67.41 / 67.59	5.81 / 5.96	3.71 / 3.94	184-185 (ethanol)	82
66	$C_{14}H_{15}NO_3$	68.01 / 68.55	5.97 / 6.16	5.52 / 5.71	—*	64
67	$C_{16}H_{19}NO_3$	70.01 / 70.31	6.88 / 7.01	4.92 / 5.13	—*	67
68	$C_{19}H_{17}NO_3$	73.98 / 74.25	5.83 / 5.57	4.57 / 4.56	118-119 (ether)	88
69	$C_{20}H_{19}NO_3$	74.44 / 74.75	5.86 / 5.96	4.21 / 4.36	—*	81
70	$C_{19}H_{16}BrNO_3$	58.81 / 59.08	3.95 / 4.18	3.47 / 3.63	—*	78
71	$C_{19}H_{16}FNO_3$	70.38 / 70.14	4.97 / 4.96	4.03 / 4.31	—*	68
72	$C_{19}H_{16}NFO_3$	69.87 / 70.14	4.81 / 4.96	4.22 / 4.31	—*	69
73	$C_{20}H_{19}NO_4$	71.88 / 71.20	5.76 / 5.68	4.11 / 4.15	—*	74

* Viscous oil.

In the work-up of the final stage – cyclization of the cyclopropyl-substituted carbinols into the corresponding 4H-3,1-benzoxazines – we feared in principle the isomeric conversion of the cyclopropyl-substituted carbenium ions (types **I-III**), which might generated in the conditions of the acid-catalyzed cyclization*. However our results showed that with use of the relatively weak trifluoroacetic acid (pK_a 0.23) in an organic solvent ($CHCl_3$) as initiator of cyclization, the conversion of the cyclopropyl-substituted carbinols into the corresponding substituted 4H-3,1-benzoxazines was not accompanied by the formation of important amounts of products of modification of the cyclopropyl fragments, and high yields of the desired heterocycles were obtained (Table 1).



35–**40**, **47**–**52** R–R^1 = OCH_2CH_2O; **35**, **47** R^2 = cyclopropyl, **36**, **48** R^2 = 2-furyl, **37**, **49** R^2 = 2-thienyl, **38**, **50** R^2 = *o*-BrC_6H_4, **39**, **51** R^2 = *p*-FC_6H_4, **40**, **52** R^2 = *m*-FC_6H_4; **41**–**46**, **53**–**57** R = R^1 = OMe; **41**, **53** R^2 = cyclopropyl, **42**, **54** R^2 = 2-furyl, **43**, **55** R^2 = 2-thienyl, **44**, **56** R^2 = *o*-FC_6H_4, **45**, **57** R^2 = *p*-FC_6H_4, **46** R^2 = *p*-$MeOC_6H_4OCH_2$



58, **66** R^3 = Me; **59**, **67** R^3 = *i*-Pr; **60**, **68** R^3 = Ph; **61**, **69** R^3 = *p*-MeC_6H_4; **62**, **70** R^3 = *p*-BrC_6H_4; **63**, **71** R^3 = *o*-FC_6H_4; **64**, **72** R^3 = *m*-FC_6H_4; **65**, **73** R^3 = *p*-$MeOC_6H_4$

* Examples of isomeric conversions of cyclopropylmethyl cations under the reaction conditions are well known, cf. [9].

Table 2. ^{1}H NMR Spectra of Compounds **7-18**, **27-73**

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)*
1	2
7	0.82 (4H, m), 1.03 (4H, m), 1.63 (1H, m), 2.82 (1H, m) – cyclopropane protons; 4.26 (2H, m), 4.35 (2H, m) – OCH_2CH_2O; 7.75 (1H, s, H-5); 7.96 (1H, s, H-8); 11.61 (1H, s, NH)
8	1.02 (2H, m); 1.09 (2H, m); 2.91 (1H, m) – cyclopropane protons; 4.31 (2H, m); 4.41 (2H, m) – OCH_2CH_2O; 6.72 (1H, m); 7.22 (1H, d, *J* = 2.4); 7.98 (1H, d, *J* = 1.8) – furane protons; 7.88 (1H, s, H-5); 8.25 (1H, s, H-8); 12.51 (1H, s, NH)
9	1.03 (2H, m); 1.11 (2H, m); 2.91 (1H, m) – cyclopropane protons; 4.31 (2H, m); 4.41 (2H, m) – OCH_2CH_2O; 7.27 (1H, m); 7.72 (1H, d, *J* = 2.6); 7.91 (1H, d, *J* = 3.2) – thiophene protons; 7.86 (1H, s, H-5); 8.11 (1H, s, H-8); 12.48 (1H, s, NH)
10	1.01 (4H, m); 2.85 (1H, m) – cyclopropane protons; 4.29 (2H, m); 4.41 (2H, m) – OCH_2CH_2O; 7.45 (1H, t, *J* = 7.4); 7.52 (1H, t, *J* = 7.2); 7.59 (1H, d, *J* = 8.0); 7.73 (1H, d, *J* = 8.0) – ArH; 7.82 (1H, s, H-5); 8.11 (1H, s, H-8); 11.79 (1H, s, NH)
11	1.05 (2H, m); 1.11 (2H, m); 2.92 (1H, m) – cyclopropane protons; 4.29 (2H, m); 4.42 (2H, m) – OCH_2CH_2O; 7.51 (2H, m); 7.88 (2H, m) – ArH; 7.86 (1H, s, H-5); 8.21 (1H, s, H-8); 12.47 (1H, s, NH)
12	1.03 (2H, m); 1.11 (2H, m); 2.91 (1H, m) – cyclopropane protons; 4.31 (2H, m); 4.42 (2H, m) – OCH_2CH_2O; 7.51 (1H, m); 7.66 (2H, m); 7.75 (1H, m) – ArH; 7.89 (1H, s, H-5); 8.21 (1H, s, H-8); 12.51 (1H, s, NH)
13	0.85 (4H, m); 1.09 (4H, m); 1.69 (1H, m); 2.92 (1H, m) – cyclopropane protons; 3.81 (3H, s, CH_3O); 3.84 (3H, s, CH_3O); 7.65 (1H, s, H-3); 8.19 (1H, s, H-6); 11.88 (1H, s, NH)
14	1.06 (2H, m); 1.12 (2H, m); 3.01 (1H, m) – cyclopropane protons; 3.88 (6H, s, $2CH_3O$); 6.71 (1H, m); 7.22 (1H, d, *J* = 5.6); 8.01 (1H, d, *J* = 3.8) – furane protons; 7.79 (1H, s, H-3); 8.48 (1H, s, H-6); 12.78 (1H, s, NH)
15	1.04 (2H, m); 1.12 (2H, m); 3.01 (1H, m) – cyclopropane protons; 3.86 (6H, s, $2CH_3O$); 7.28 (1H, d. t, J_1 = 4.8, J_2 = 4.2); 7.75 (1H, d, *J* = 4.2); 7.93 (1H, d, *J* = 4.8) – thiophene protons; 7.74 (1H, s, H-3); 8.32 (1H, s, H-6); 12.71 (1H, s, NH)
16	1.05 (4H, m); 2.96 (1H, m) – cyclopropane protons; 3.88 (3H, s, CH_3O); 3.90 (3H, s, CH_3O); 7.38 (1H, m); 7.42 (1H, m); 7.66 (1H, m); 7.88 (1H, m) – ArH; 7.75 (1H, s, H-3); 8.47 (1H, s, H-6); 12.43 (1H, s, NH)
17	1.04 (2H, m), 1.12 (2H, m), 3.01 (1H, m) – cyclopropane protons; 3.87 (3H, s, CH_3O); 3.89 (3H, s, CH_3O); 7.44 (2H, m), 7.99 (2H, m) – ArH; 7.75 (1H, s, H-3); 8.42 (1H, s, H-6); 12.68 (1H, s, NH)
18	1.07 (2H, m), 1.31 (2H, m), 2.61 (1H, m) – cyclopropane protons; 3.81 (3H, s, CH_3O); 3.95 (3H, s, CH_3O); 4.05 (3H, s, CH_3O); 4.61 (2H, s, CH_2O); 6.88 (2H, d, *J* = 8.9), 7.05 (2H, d, *J* = 8.9) – ArH; 7.56 (1H, s, H-3), 8.57 (1H, s, H-6); 12.72 (1H, s, NH)
27	0.82 (4H, m), 1.69 (1H, m) – cyclopropane protons; 2.55 (3H, s, CH_3); 4.24 (2H, m); 4.35 (2H, m) – OCH_2CH_2O; 7.52 (1H, s, H-5); 8.01 (1H, s, H-8); 11.68 (1H, s, NH)
28	0.82 (4H, m), 1.71 (1H, m) – cyclopropane protons; 1.09 (6H, d, *J* = 6.4, $2CH_3$); 3.63 (1H, m, $CH(CH_3)_2$); 4.27 (2H, m), 4.33 (2H, m) – OCH_2CH_2O; 7.54 (1H, s, H-5); 7.93 (1H, s, H-8); 11.71 (1H, s, NH)
29	1.11 (4H, m), 1.51 (1H, m) – cyclopropane protons; 4.26 (2H, m), 4.34 (2H, m) – OCH_2CH_2O; 6.88 (1H, s), 7.30 (1H, s) – H-5,8; 7.49 (2H, t, *J* = 7.6), 7.61 (3H, m) – ArH; 10.38 (1H, s, NH)
30	0.64 (4H, m), 1.52 (1H, m) – cyclopropane protons; 2.38 (3H, s, CH_3); 4.25 (2H, m), 4.33 (2H, m) – OCH_2CH_2O; 6.87 (1H, s), 7.28 (1H, s) – H-5,8; 7.29 (2H, d, *J* = 8.2), 7.52 (2H, d, *J* = 8.2) – ArH; 10.31 (1H, s, NH)
31	0.53 (2H, m), 0.62 (2H, m), 1.48 (1H, m) – cyclopropane protons; 4.27 (2H, m), 4.33 (2H, m) – OCH_2CH_2O; 6.89 (1H, s), 7.18 (1H, s) – H-5,8; 7.52 (2H, d, *J* = 8.2), 7.70 (2H, d, *J* = 8.2) – ArH; 10.25 (1H, s, NH)
32	0.72 (4H, m), 1.61 (1H, m) – cyclopropane protons; 4.25 (2H, m), 4.35 (2H, m) – OCH_2CH_2O; 6.88 (1H, s), 7.61 (1H, s) – H-5,8; 7.32 (2H, m), 7.51 (1H, m), 7.62 (1H, m) – ArH; 10.88 (1H, s, NH)

Table 2 (continued)

1	2
33	0.54 (2H, m), 0.62 (2H, m), 1.48 (1H, m) – cyclopropane protons; 4.27 (2H, m), 4.35 (2H, m) – OCH_2CH_2O; 6.91 (1H, s), 7.18 (1H, s) – H-5,8; 7.34 (1H, m), 7.41 (1H, m), 7.46 (1H, m), 7.53 (1H, m) – ArH; 10.31 (1H, s, NH)
34	0.85 (2H, m), 1.09 (2H, m), 1.61 (1H, m) – cyclopropane protons; 3.91 (3H, s, CH_3O); 4.25 (2H, m), 4.36 (2H, m) – OCH_2CH_2O; 6.95 (2H, d, J = 8.7), 7.71 (2H, d, J = 8.7) – ArH; 7.11 (1H, s), 8.21 (1H, s) – H-5,8; 11.09 (1H, s, NH)
35	0.25 (1H, m), 0.45 (1H, m), 0.61 (1H, m), 0.72 (1H, m), 0.79 (2H, m), 1.05 (2H, m), 1.35 (1H, m), 1.48 (1H, m) – cyclopropane protons; 2.75 (1H, br. s, OH); 3.89 (1H, d, J = 8.6, CH-benzyl); 4.24 (4H, s, OCH_2CH_2O); 6.81 (1H, s), 7.62 (1H, s) – H-5,8; 9.01 (1H, s, NH)
36	1.22 (1H, m), 0.38 (2H, m), 0.51 (1H, m), 1.12 (1H, m) – cyclopropane protons; 4.01 (1H, d, J = 7.6, CH-benzyl); 4.22 (4H, m, OCH_2CH_2O); 6.01 (1H, s, OH); 6.71 (1H, m), 7.18 (1H, d, J = 3.2), 7.91 (1H, m) – furane protons; 6.82 (1H, s), 7.62 (1H, s) – H-5,8; 10.42 (1H, s, NH)
37	0.23 (1H, m), 0.37 (2H, m), 0.48 (1H, m), 1.25 (1H, m) – cyclopropane protons; 4.21 (1H, d, J = 10.6, CH-benzyl); 5.95 (1H, s, OH); 4.25 (4H, s, OCH_2CH_2O); 6.88 (1H, s), 7.45 (1H, s) – H-5,8; 7.23 (1H, dd, J_1 = 5.8, J_2 = 3.8), 7.71 (1H, d, J = 3.8), 7.85 (1H, d, J = 5.8) – thiophene protons; 10.35 (1H, s, NH)
38	0.31 (1H, m), 0.42 (1H, m), 0.69 (2H, m), 1.41 (1H, m) – cyclopropane protons; 2.45 (1H, br. s, OH); 3.96 (1H, d, J = 9.2, CH-benzyl); 4.27 (4H, m, OCH_2CH_2O); 6.85 (1H, s), 7.86 (1H, s) – H-5,8; 7.30 (1H, m), 7.38 (1H, m), 7.55 (1H, m), 7.66 (1H, m) – ArH; 9.21 (1H, s, NH)
39	0.21 (1H, m), 0.41 (2H, m), 0.56 (1H, m), 1.26 (1H, m) – cyclopropane protons; 3.91 (1H, d, J = 9.4, CH-benzyl); 4.23 (4H, m, OCH_2CH_2O); 5.11 (1H, br. s, OH); 6.73 (1H, s), 7.55 (1H, s) – H-5,8; 7.10 (2H, m), 7.92 (2H, m) – ArH; 10.41 (1H, s, NH)
40	0.15 (1H, m), 0.41 (2H, m), 0.55 (1H, m), 1.24 (1H, m) – cyclopropane protons; 3.86 (1H, d, J = 8.2, CH-benzyl); 4.15 (4H, m, OCH_2CH_2O); 5.35 (1H, br. s, OH); 6.71 (1H, s), 7.85 (1H, s) – H-5,8; 7.10 (1H, m), 7.36 (1H, m), 7.59 (1H, m), 7.65 (1H, m) – ArH; 10.41 (1H, br. s, NH)
41	0.26 (1H, m), 0.31 (1H, m), 0.39 (1H, m), 0.42 (1H, m), 0.75 (1H, m), 1.11 (1H, m), 1.72 (1H, m) – cyclopropane protons; 3.71 (3H, s, CH_3O); 3.76 (3H, s, CH_3O); 4.25 (1H, d, J = 9.6, CH-benzyl); 5.42 (1H, s, OH); 6.96 (1H, s), 7.22 (1H, s) – H-3,6; 9.63 (1H, s, NH)
42	0.26 (1H, m), 0.34(1H, m), 0.41 (1H, m), 0.49 (1H, m), 1.16 (1H, m) – cyclopropane protons; 3.51 (6H, s, $2CH_3O$); 4.12 (1H, d, J = 9.8, CH-benzyl); 5.95 (1H, s, OH); 6.71 (1H, m), 7.18 (1H, d, J = 4.0), 7.94 (1H, m) – furane protons; 6.93 (1H, s), 7.79 (1H, s) – H-3,6; 10.46 (1H, s, NH)
43	0.27 (1H, m), 0.38 (2H, m), 0.47 (1H, m), 1.17 (1H, m) – cyclopropane protons; 3.74 (3H, s, CH_3O); 3.76 (3H, s, CH_3O); 4.22 (1H, d, J = 8.4, CH-benzyl); 5.88 (1H, s, OH); 6.97 (1H, s), 7.50 (1H, s) – H-3,6; 7.24 (1H, dd, J_1 = 5.8, J_2 = 3.2), 7.76 (1H, d, J = 3.2), 7.87 (1H, d, J = 5.8) – thiophene protons; 10.41 (1H, s, NH)
44	0.28 (1H, m), 0.34 (2H, m), 0.48 (1H, m), 1.19 (1H, m) – cyclopropane protons; 3.75 (6H, s, $2CH_3O$); 4.18 (1H, d, J = 9.6, CH-benzyl); 5.76 (1H, s, OH); 6.96 (1H, s), 7.65 (1H, s) – H-3,6; 7.37 (2H, m), 7.62 (1H, m), 7.84 (1H, m) – ArH; 10.31 (1H, s, NH)
45	0.25 (1H, m), 0.38 (2H, m), 0.48 (1H, m), 1.19 (1H, m) – cyclopropane protons; 3.72 (3H, s, CH_3O); 3.74 (3H, s, CH_3O); 4.21 (1H, d, J = 7.3, CH-benzyl); 5.91 (1H, s, OH); 6.97 (1H, s), 7.61 (1H, s) – H-3,6; 7.39 (2H, m), 7.99 (2H, m) – ArH; 10.42 (1H, s, NH)
46	0.15 (1H, m), 0.41 (2H, m), 0.55 (1H, m), 1.15 (1H, m) – cyclopropane protons; 3.65 (1H, d, J = 8.6, CH-benzyl); 3.81 (3H, s, CH_3O); 3.87 (3H, s, CH_3O); 3.95 (3H, s, CH_3O); 4.61 (2H, dd, J_1 = 34.4, J_2 = 17.2, CH_2O); 5.26 (1H, s, OH); 6.57 (1H, s), 8.12 (1H, s) – H-3,6; 6.87 (2H, d, J = 8.2), 6.97 (2H, d, J = 8.2) – ArH; 10.21 (1H, s, NH)
47	0.38 (2H, m), 0.62 (2H, m), 0.84 (2H, m), 1.04 (2H, m), 1.21 (1H, m), 1.69 (1H, m) – cyclopropane protons; 4.21 (4H, m, OCH_2CH_2O); 4.37 (1H, d, J = 8.4, H-4); 6.58 (1H, s), 6.67 (1H, s) – H-5,8
48	0.45 (1H, m), 0.52 (1H, m), 0.64 (2H, m), 1.32 (1H, m) – cyclopropane protons; 4.23 (4H, m, OCH_2CH_2O); 4.62 (1H, d, J = 8.2, H-4); 6.49 (1H, dd, J_1 = 4.2, J_2 = 1.8), 7.03 (1H, d, J = 4.2), 7.57 (1H, d, J = 1.8) – furane protons; 6.68 (1H, s), 6.89 (1H, s) – H-5,8

Table 2 (continued)

1	2
49	0.47 (1H, m), 0.57 (1H, m), 0.72 (2H, m), 1.38 (1H, m) – cyclopropane protons; 4.25 (4H, m, OCH_2CH_2O); 4.65 (1H, d, J = 8.3, H-4); 6.69 (1H, s); 6.84 (1H, s) – H-5, H-8; 7.10 (1H, dd, J_1 = 4.4, J_2 = 3.8); 7.46 (1H, dd, J_1 = 4.4, J_2 = 1.2); 7.73 (1H, dd, J_1 = 3.8, J_2 = 1.2) – thiophene protons
50	0.55 (1H, m), 0.66 (1H, m), 0.75 (1H, m), 0.83 (1H, m), 1.45 (1H, m) – cyclopropane protons; 4.26 (4H, m, OCH_2CH_2O); 4.72 (1H, d, J = 8.8, H-4); 6.82 (1H, s), 6.88 (1H, s) – H-5,8; 7.28 (1H, dt, J_o = 7.8, J_m = 1.8), 7.37 (1H, dt, J_o = 7.8, J_m = 1.4), 7.64 (1H, dd, J_o = 7.8, J_m = 1.4), 7.70 (1H, dd, J_o = 7.8, J_m = 1.8) – ArH
51	0.48 (1H, m), 0.61 (1H, m), 0.73 (2H, m), 1.38 (1H, m) – cyclopropane protons; 4.27 (4H, m, OCH_2CH_2O); 4.67 (1H, d, J = 8.2, H-4); 6.71 (1H, s), 6.85 (1H, s) – H-5,8; 7.14 (2H, m), 8.15 (2H, m) – ArH
52	0.47 (1H, m), 0.61 (1H, m), 0.72 (2H, m), 1.36 (1H, m) – cyclopropane protons; 4.26 (4H, m, OCH_2CH_2O); 4.65 (1H, d, J = 8.6, H-4); 6.72 (1H, s), 6.87 (1H, s) – H-5,8; 7.17 (1H, m), 7.40 (1H, m), 7.82 (1H, m), 7.93 (1H, m) – ArH
53	0.40 (2H, m), 0.61 (2H, m), 0.81 (2H, m), 1.05 (2H, m), 1.25 (1H, m), 1.71 (1H, m) – cyclopropane protons; 3.82 (3H, s, CH_3O); 3.86 (3H, s, CH_3O); 4.48 (1H, d, J = 8.1, H-4); 6.55 (1H, s), 6.71 (1H, s) – H-5 and H-8
54	0.45 (1H, m), 0.55(1H, m), 0.69 (2H, m), 1.63 (1H, m) – cyclopropane protons; 3.86 (3H, s, CH_3O); 3.88 (3H, s, CH_3O); 4.74 (1H, d, J = 8.6, H-4); 6.64 (1H, s), 6.95 (1H, s) – H-5,8; 6.52 (1H, dd, J_1 = 3.8, J_2 = 2.8), 7.05 (1H, d, J = 3.8), 7.59 (1H, m)
55	0.46 (1H, m), 0.52 (1H, m), 0.67 (2H, m), 1.38 (1H, m) – cyclopropane protons; 3.88 (3H, s, CH_3O); 3.92 (3H, s, CH_3O); 4.75 (1H, d, J = 8.2, H-4); 6.65 (1H, s), 6.87 (1H, s) – H-5,8; 7.11 (1H, dd, J_1 = 4.8, J_2 = 4.2), 7.54 (1H, dd, J_1 = 4.8, J_2 = 1.4), 7.63 (1H, dd, J_1 = 4.2, J_2 = 1.4)
56	0.48 (1H, m), 0.58 (1H, m), 0.71 (2H, m), 1.41 (1H, m) – cyclopropane protons; 3.86 (3H, s, CH_3O); 3.90 (3H, s, CH_3O); 4.78 (1H, d, J = 7.8, H-4); 6.61 (1H, s), 6.66 (1H, s) – H-5,8; 7.11-7.22 (2H, m), 7.48 (1H, m), 7.94 (1H, m) – ArH
57	0.48 (1H, m), 0.56 (1H, m), 0.69 (2H, m), 1.38 (1H, m) – cyclopropane protons; 3.89 (3H, s, CH_3O); 3.93 (3H, s, CH_3O); 4.74 (1H, d, J = 8.3, H-4); 6.67 (1H, s), 6.89 (1H, s) – H-5,8; 7.13 (2H, m), 8.15 (2H, m) – ArH
58	0.74 (4H, m), 1.75 (1H, m) – cyclopropane protons; 1.25 (3H, d, J = 6.8); 4.21 (4H, m, OCH_2CH_2O); 4.81 (1H, dq, J_1 = 6.8, J2 = 2.0, CH-benzoic); 5.28 (1H, d, J = 2.0, OH), 6.84 (1H, s), 6.96 (1H, s) – H-5,8; 9.51 (1H, s, NH)
59	0.74 (6H, d, J = 6.2, $CH(CH_3)_2$); 0.86 (4H, m), 1.72 (1H, m) – cyclopropane protons; 1.79 (1H, m, $CH(CH_3)_2$); 4.21 (4H, m, OCH_2CH_2O); 4.40 (1H, d, J = 5.8, CH-benzoic); 5.46 (1H, s, OH), 6.77 (1H, s), 7.04 (1H, s) – H-5,8; 9.53 (1H, s, NH)
60	0.71 (4H, m), 1.71 (1H, m) – cyclopropane protons; 4.19 (4H, m, OCH_2CH_2O); 5.83 (1H, d, J = 2.2, OH); 6.06 (1H, d, J = 2.2, CH-benzyl); 6.81 (1H, s), 6.99 (1H, s) – H-5,8; 7.19 (2H, m), 7.29 (4H, m) – ArH; 9.48 (1H, s, NH)
61	0.72 (4H, m), 1.69 (1H, m) – cyclopropane protons; 2.25 (3H, s, CH_3); 4.19 (4H, m, OCH_2CH_2O); 5.79 (1H, d, J = 2.0, OH); 5.98 (1H, d, J = 2.0, CH-benzyl); 6.79 (1H, s), 7.01 (1H, s) – H-5,8; 7.08 (2H, d, J = 8.8), 7.16 (2H, d, J = 8.8) – ArH; 9.48 (1H, s, NH)
62	0.62 (1H, m), 0.74 (3H, m), 1.69 (1H, m) – cyclopropane protons; 4.21 (4H, m, OCH_2CH_2O); 5.81 (1H, d, J = 2.8, OH); 6.09 (1H, d, J = 2.8, CH-benzyl); 6.83 (1H, s), 6.93 (1H, s) – H-5,8; 7.22 (2H, d, J = 7.8), 7.46 (2H, d, J = 7.8) – ArH; 9.42 (1H, s, NH)
63	0.63 (1H, m), 0.72 (3H, m), 1.72 (1H, m) – cyclopropane protons; 4.21 (4H, m, OCH_2CH_2O); 6.01 (1H, br. s, OH); 6.08 (1H, d, J = 5.8, CH-benzyl); 6.79 (1H, s), 7.02 (1H, s) – H-5,8; 7.08 (1H, m), 7.16 (1H, m), 7.28 (1H, m), 7.39 (1H, m) – ArH; 9.42 (1H, s, NH)
64	0.65 (2H, m), 0.75 (1H, m), 0.91 (1H, m), 1.37 (1H, m) – cyclopropane protons; 4.15 (4H, m, OCH_2CH_2O); 5.68 (1H, d, J = 7.8, CH-benzyl); 5.81 (1H, br. s, OH); 6.51 (1H, s), 7.35 (1H, s) – H-5,8; 6.85 (1H, m), 7.06 (2H, m), 7.21 (1H, m) – ArH; 9.01 (1H, s, NH)
65	0.64 (2H, m), 0.79 (2H, m) and 1.45 (1H, m) – cyclopropane protons; 3.72 (3H, s, CH_3O); 4.11 (4H, m, OCH_2CH_2O); 5.67 (1H, s, CH-benzyl); 5.95 (1H, br. s, OH); 6.51 (1H, s), 7.33 (1H, s) – H-5,8; 6.76 (2H, d, J = 8.0), 7.19 (2H, d, J = 8.0) – ArH; 9.24 (1H, s, NH)

Table 2 (continued)

1	2
66	0.81 (2H, m), 0.99 (2H, m), 1.67 (1H, m) – cyclopropane protons; 1.45 (3H, d, *J* = 6.8, CH_3); 4.24 (4H, m, OCH_2CH_2O); 5.19 (1H, q, *J* = 6.8, H-4); 6.45 (1H, s), 6.67 (1H, s) – H-5,8
67	0.81 (2H, m), 1.01 (2H, m), 1.65 (1H, m) – cyclopropane protons; 0.86 (3H, d, *J* = 7.1), 0.95 (3H, d, *J* = 7.1) – $CH(C\underline{H}_3)_2$; 1.95 (1H, m, $C\underline{H}(CH_3)_2$); 4.22 (4H, s, OCH_2CH_2O); 4.90 (1H, d, *J* = 4.4, H-4); 6.37 (1H, s), 6.63 (1H, s) –H-5,8
68	0.70-0.91 (3H, m), 1.01 (1H, m), 1.68 (1H, m) – cyclopropane protons; 4.21 (4H, m, OCH_2CH_2O); 6.07 (1H, s, H-4); 6.24 (1H, s), 6.73 (1H, s) – H-5,8; 7.27 (2H, m), 7.38 (3H, m) – ArH
69	0.68-0.87 (3H, m), 1.01 (1H, m), 1.65 (1H, m) – cyclopropane protons; 2.35 (3H, s, CH_3); 4.32 (4H, m, OCH_2CH_2O); 6.01 (1H, s, H-4); 6.23 (1H, s), 6.74 (1H, s) – H-5,8; 7.16 (4H, m, ArH)
70	0.71–0.91 (3H, m), 1.02 (1H, m), 1.67 (1H, m) – cyclopropane protons; 4.23 (4H, m, OCH_2CH_2O); 6.02 (1H, s, H-4); 6.21 (1H, s), 6.74 (1H, s) – H-5,8; 7.14 (2H, d, *J* = 8.4), 7.51 (2H, d, *J* = 8.4) – ArH
71	0.70–0.92 (3H, m), 1.05 (1H, m), 1.73 (1H, m) – cyclopropane protons; 4.22 (4H, m, OCH_2CH_2O); 6.26 (1H, s, H-4); 6.45 (1H, s), 6.77 (1H, s) – H-5,8; 7.11 (3H, m), 7.32 (1H, m) – ArH
72	0.71–0.92 (3H, m), 1.03 (1H, m), 1.67 (1H, m) – cyclopropane protons; 4.23 (4H, m, OCH_2CH_2O); 6.04 (1H, s, H-4); 6.24 (1H, s), 6.75 (1H, s) – H-5,8; 6.97 (1H, m), 7.05 (2H, m), 7.34 (1H, m) – ArH
73	0.72 (1H, m), 0.82 (1H, m), 1.01 (1H, m), 1.65 (1H, m) – cyclopropane protons; 3.80 (3H, s, CH_3O); 4.24 (4H, m, OCH_2CH_2O); 6.01 (1H, s, H-4); 6.24 (1H, s), 6.73 (1H, s) – H-5,8; 6.88 (2H, d, *J* = 8.3), 7.19 (2H, d, *J* = 8.3) – ArH

* ^{1}H NMR spectra of compounds **7-12**, **13-17**, **27-33**, **36**, **41-45**, and **58-63** were recorded in DMSO-d_6, compounds **18**, **34**, **38-40**, **46**, **64**, and **65** in $CDCl_3$.

Only in the case of the amido alcohol **46,** its interaction with trifluoroacetic acid under the reaction conditions did not lead to the corresponding 4H-3,1-benzoxazine **74**; the reaction completed with the formation of the expected product of the isomerization of the cyclopropane unit in the starting alcohol **46** into the β-hydroxybutenyl (compound **75**).

On acid-catalyzed heterocyclization of the cyclopropyl-substituted amido alcohols **35-45** and **58-65** the 4H-3,1-benzoxazines were formed without modification of the three-carbon ring. This may indicate that in the conversion process the "open" cyclopropylcarbenium ions (type I) are not formed, and the reaction occurs trough intermediate cyclopropyl-substituted 3,1-benzoxazininium ion (types I and II). Evidently elimination of the protonated hydroxy groups from the benzyl position of the amido alcohols **35-45** and **58-65** occurs with nucleophilic assistance of the oxygen atom of the amide unit*, as a consequence of which the more stable (relative to an ion of type I) cyclic ion II is formed directly, leading to formation of the cyclopropyl-substituted benzoxazines **47-57** and **66-73**.

As for the anomalous, at first glance, conversion of the amido alcohol **46** into unsaturated amido alcohol **75**, we suggest that it can be connected to the presence in the substrate of two potentially nucleophilic centers, both of which participate in nucleophilic assistance in removal of the protonated hydroxy group from alcohol **46**. Since the nucleophilic properties of the "ester" oxygen are expressed more strongly than those of the oxygen

* Similar nucleophilic assistance by the *ortho*-substituent of the acid-catalyzed opening of cyclopropane ring was observed, for example in [10, 11].

atom of the carbonyl group of the amide substituent, it may be suggested that, at least in the first step this conversion proceeds *via* the cyclopropyl-substituted cyclic benzoxazepinium ion **V**. As has been shown elsewhere [12, 13] similar seven-membered cyclic ions are considerably less stable than their six-membered isomeric ions. Since the isomeric conversion of benzoxazepinium into benzoxazinium ions occurs *via* carbenium ions of the open structure [12, 13] it may be accepted that cyclic benzoxazepinium ions of type **V** are the sources of ions of type **VI** which are capable of conversion into the unsaturated amido alcohol **75**.

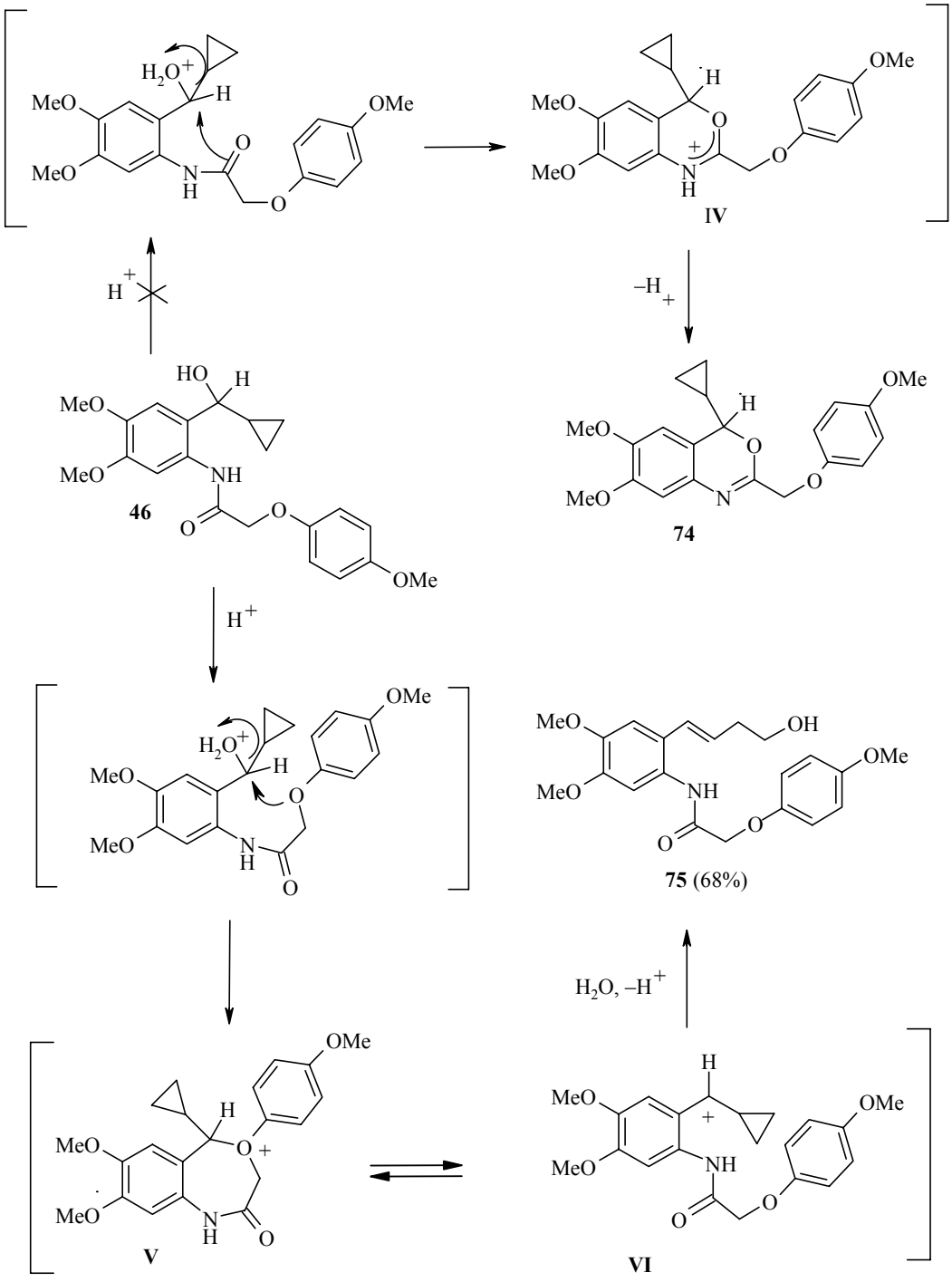


Table 3. Mass Spectra of the Compounds Synthesized

Compound	*m/z* (I_{rel}, %)
7	287 $[M]^+$ (69.1); 219 (98.0); 190 (9.1); 163 (12.2); 135 (11.2); 94 (9.5); 69 (53.2); 41 (100.0)
8	313 $[M]^+$ (100.0); 272 (68.0); 244 (99.5); 218 (23.8); 204 (68.5); 190 (37.1); 178 (20.6); 162 (12.3); 134 (20.6); 106 (13.5); 95 (98.3); 76 (16.1); 69 (52.1); 39 (97.5)
9	329 $[M]^+$ (99.5); 288 (52.6); 260 (98.9); 228 (10.6); 218 (14.9); 204 (34.3); 190 (10.6); 178 (9.6); 111 (100.0); 83 (20.5); 69 (12.6); 39 (57.8)
10	401* $[M]^+$ (76.3); 332* (22.2); 183* (100.0); 155* (53.2); 139 (18.3); 76 (38.8); 69 (19.3); 50 (21.2); 41 (39.9); 39 (29.9)
11	341 $[M]^+$ (21.2); 272 (6.9); 123 (100.0); 95 (52.6)
12	341 $[M]^+$ (100.0); 300 (18.3); 272 (19.4); 123 (50.1); 95 (31.3)
13	289 $[M]^+$ (40.5); 221 (42.1); 206 (43.2); 69 (53.5); 41 (100.0)
14	315 $[M]^+$ (32.1); 246 (6.1); 95 (100.0); 69 (11.2); 39 (54.5)
15	331 $[M]^+$ (36.1); 262 (7.8); 111 (100.0); 83 (12.1); 39 (29.2)
16	343 $[M]^+$ (36.1); 274 (7.1); 123 (100.0); 95 (65.4); 75 (20.1); 69 (7.2); 39 (16.2)
17	343 $[M]^+$ (25.1); 274 (7.1); 123 (100.0); 95 (65.4); 75 (20.1); 69 (7.2); 39 (16.2)
27	261 $[M]^+$ (50.1); 193 (100.0); 178 (23.6); 137 (22.8); 94 (11.5); 69 (31.1); 41 (63.2)
28	289 $[M]^+$ (16.5); 246 (54.6); 204 (9.8); 178 (29.8); 94 (8.1); 69 (51.2); 41 (100.0)
29	323 $[M]^+$ (29.8); 255 (41.5); 169 (8.7); 143 (12.2); 94 (12.1); 77 (39.1); 69 (54.2); 41 (100.0)
30	337 $[M]^+$ (32.1); 269 (63.3); 183 (9.1); 157 (8.5); 119 (11.2); 91 (27.3); 69 (45.6); 41 (100.0)
31	401* $[M]^+$ (22.3); 333* (29.8); 94 (9.9); 69 (51.1); 41 (100.0)
32	341 $[M]^+$ (30.8); 273 (60.3); 161 (12.2); 123 (21.2); 94 (20.8); 69 (59.2); 41 (100.0)
33	341 $[M]^+$ (28.2); 273 (50.5); 161 (9.1); 123 (10.1); 95 (19.2); 69 (41.2); 41 (100.0)
36	315 $[M]^+$ (11.2); 287 (7.5); 272 (8.1); 204 (6.2); 178 (7.4); 164 (6.1); 95 (100.0); 69 (9.1); 51 (10.1); 39 (68.3)
37	331 $[M]^+$ (20.1); 303 (9.5); 288 (10.1); 272 (8.1); 260 (8.3); 220 (9.5); 204 (7.9); 192 (7.1); 111 (100.0); 95 (6.1); 83 (9.5); 68 (9.4); 39 (40.4)
41	291 $[M]^+$ (87.1); 273 (10.2); 263 (31.1); 248 (19.8); 223 (21.5); 206 (38.1); 195 (42.1); 180 (32.1); 162 (12.6); 69 (82.5); 41 (100.0)
42	317 $[M]^+$ (22.5); 289 (11.5); 274 (14.9); 206 (9.1); 95 (100.0); 69 (10.1); 39 (46.5)
43	333 $[M]^+$ (10.1); 290 (8.5); 206 (8.1); 111 (100.0); 83 (10.1); 69 (9.8); 39 (28.1)
44	345 $[M]^+$ (6.3); 302 (8.1); 274 (6.1); 206 (8.5); 123 (100.0); 95 (39.2); 69 (8.2); 41 (9.1)
45	345 $[M]^+$ (34.7); 317 (16.1); 302 (19.5); 286 (11.2); 274 (12.1); 206 (14.5); 123 (100.0); 95 (72.5); 75 (22.5); 41 (19.5)
58	263 $[M]^+$ (11.2); 230 (9.5); 193 (10.4); 178 (47.1); 163 (26.2); 152 (11.9); 121 (18.5); 93 (10.9); 69 (49.1); 41 (100.0)
59	291 $[M]^+$ (18.5); 248 (26.1); 220 (18.8); 206 (8.2); 180 (36.6); 163 (20.1); 152 (8.3); 123 (8.1); 94 (11.6); 69 (100.0); 41 (69.5)
60	325 $[M]^+$ (3.2); 240 (14.1); 105 (20.1); 77 (22.3); 69 (43.1); 41 (100.0)
61	339 $[M]^+$ (10.3); 270 (7.8); 254 (40.2); 178 (8.1); 163 (12.5); 119 (26.1); 91 (19.9); 77 (9.2); 69 (50.4); 41 (100)
62	403* $[M]^+$ (4.1); 318* (20.1); 183* (12.1); 163 (14.2); 94 (6.9); 77 (10.1); 69 (53.2); 41 (100.0)
63	343 $[M]^+$ (11.1); 325 (12.3); 258 (52.1); 237 (12.9); 163 (20.5); 123 (29.2); 95 (12.1); 69 (51.1); 41 (100.0)

* Peaks with maximum intensity in clusters of ions containing bromine.

In no case have we observed isomeric conversion of the three-carbon ring on the amide group in the carbinols **35**, **41**, **58-65**. This may indicate that in the cyclic intermediates (types **II**, **III**) the position of the positive charge on the carbon atom, bonded to the cyclopropane unit, is delocalized on the N–C–O triad, which provides greater stability under the conditions of acid-catalyzed cyclization.

EXPERIMENTAL

^{1}H NMR spectra were recorded with Bruker ORX 500 (500 MHz) and Varian VXR-400 (400 MHz) in $CDCl_3$ (internal standard signal of residual protons of $CHCl_3$), and DMSO-d_6 (internal standard TMS). Mass spectra were recorded with a Finnigan MAT INCOS-50, electron impact ionization, 70 eV. Control of the purity of the products was by TLC on Al_2O_3 (activity II) plates with 1:1:3 ether–chloroform–petroleum ether (40-70°C).

6-Cyclopropanoyl-1,4-benzodioxane (1) was obtained by acylation of 1,4-benzodioxane with cyclopropanecarbonyl chloride as described in [14] with a yield of 81%; mp 72-73°(ethanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.95 (2H, m); 1.11 (2H, m) – cyclopropane protons; 4.28 (4H, m, OCH_2CH_2O); 6.88 (1H, d, J = 9.2, H-8); 7.52 (2H, m, H-5,7). Found, %: C 70.31; H 5.79. $C_{12}H_{12}O_3$. Calculated, %: C 70.57; H 5.92.

4-Cyclopropanoylveratrole (2) was synthesized analogously from veratrole with a yield of 76%; mp 75-76°C (ethanol). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 0.99 (4H, m) and 2.91 (1H, m) – cyclopropane protons; 3.82 (3H, s, CH_3O); 3.87 (3H, s, CH_3O); 7.10 (1H, d, J_o = 7.8, H-5); 7.51 (1H, d, J_m = 1.9, H-2); 7.78 (1H, dd, J_o = 7.8, J_m = 1.9, H-6). Found, %: C 69.69; H 6.72. $C_{12}H_{14}O_3$. Calculated, %: C 69.88; H 6.84.

7-Cyclopropanoyl-6-nitro-1,3-benzodioxane (3) was obtained by nitration of compounds by a known method [15]. Yield 84%; mp 108-109°C (ethanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.06 (2H, m); 1.28 (2H, m); 2.11 (1H, m) – cyclopropane protons; 4.36 (4H, m, OCH_2CH_2O); 6.90 (1H, s, H-8); 7.64 (1H, s, H-5). Mass spectrum, *m/z* (I_{rel}, %): 249 $[M]^+$ (5), 208 (6), 177 (10), 149 (19), 134 (33), 121 (26), 94 (12), 78 (21), 69 (73), 50 (100), 41 (96). Found, %: C 57.69; H 4.31; N 5.41. $C_{12}H_{11}NO_5$.. Calculated, %: C 57.83; H 4.45; N 5.62.

5-Cyclopropanoyl-4-nitroveratrole (4) was obtained analogously from the cyclopropyl aryl ketone **2**. Yield 72%; mp 96-97°C (ethanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm : 1.09 (2H, m); 1.33 (2H, m); 2.10 (1H, m) – cyclopropane protons; 3.99 (6H, s, $2CH_3O$); 6.80 (1H, s, H-6); 7.62 (1H, s, H-3). Mass spectrum, *m/z* (I_{rel}, %): 251 $[M]^+$ (41), 210 (11), 194 (32), 182 (12), 164 (54), 151 (14), 136 (100), 108 (11), 93 (45), 82 (19), 69 (51), 50 (31), 41 (69). Found, %: C 57.14; H 5.03; N 5.26. $C_{12}H_{13}NO_5$. Calculated, %: C 57.37; H 5.21; N 5.58.

6-Amino-7-cyclopropanoyl-1,4-benzodioxane (5) was obtained by the reduction of nitro compound **3** as described in [15]. Yield 71%; mp 94-95°C (ethanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.92 (2H, m); 1.14 (2H, m); 2.48 (1H, m) – cyclopropane protons; 4.29 (2H, m); 4.31 (2H, m) – OCH_2CH_2O; 5.91 (2H, br. s, NH_2); 6.12 (1H, s, H-5); 7.48 (1H, s, H-8). Found, %: C 65.56; H 5.72; N 6.19. $C_{12}H_{13}NO_3$. Calculated, %: C 65.74; H 5.96; N 6.39.

4-Amino-5-cyclopropanoylveratrole (6) was obtained from the nitroderivative **4**. Yield 67%; mp 125-126°C (ethanol). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.91 (4H, m); 2.73 (1H, m) – cyclopropane protons; 3.72 (3H, s, CH_3O); 3.77 (3H, s, CH_3O); 6.34 (1H, s, H-3); 7.08 (2H, br. s, NH_2); 7.43 (1H, s, H-6). Mass spectrum, *m/z* (I_{rel}, %): 221 $[M]^+$ (91), 206 (100), 180 (12), 162 (9), 136 (10), 108 (8), 94 (48), 79 (9), 69 (23), 52 (22), 39 (1). Found, %: C 64.91; H 6.69; N 6.11. $C_{12}H_{13}NO_3$. Calculated, %: C 65.14; H 6.83; N 6.33.

7-Acyl-6-amino-1,4-benzodioxane 19-26 were obtained by reduction of the corresponding nitro compounds by the method from [15].

7-Acetyl-6-amino-1,4-benzodioxane (19). Yield 68%; mp 129-130°C (ethanol). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.41 (3H, s, CH_3); 4.15 (2H, m); 4.26 (2H, m) – OCH_2CH_2O; 5.22 (1H, s, H-5); 6.82 (2H, br. s, NH_2); 7.21 (1H, s, H-8). Mass spectrum, *m/z* (I_{rel}, %): 193 $[M]^+$ (100), 178 (57), 150 (12), 137 (69), 109 (12), 94 (92), 78 (11), 65 (14); 52 (31), 45 (53). Found, %: C 61.92; H 5.55; N 7.01. $C_{10}H_{11}NO_3$. Calculated, %: C 62.16; H 5.74; N 7.25.

6-Amino-7-isobutyroyl-1,4-benzodioxane (20). Yield 71%; mp 114-115°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.08 (6H, d, J = 5.8, $2CH_3$); 3.48 (1H, m, C<u>H</u>$(CH_3)_2$); 4.15 (2H, m); 4.25 (2H, m) – OCH_2CH_2O; 6.22 (1H, s, H-5); 6.82 (2H, br. s, NH_2); 7.24 (1H, s, H-8). Found, %: C 64.91; H 6.72; N 6.11. $C_{12}H_{15}NO_3$. Calculated, %: C 65.14; H 6.83; N 6.33.

6-Amino-7-benzoyl-1,4-benzodioxane (21). Yield 73%; mp 134-135°C (ethanol) [15].

6-Amino-7-(4-methylbenzoyl)-1,4-benzodioxane (22). Yield 82%; mp 137-138°C (ethanol). ^{1}H NMR spectrum ($CDCl_3$); δ, ppm (*J*, Hz): 2.44 (3H, s, CH_3); 4.17 (2H, m); 4.35 (2H, m) – OCH_2CH_2O; 5.85 (2H, br. s, NH_2); 6.21 (1H, s, H-5); 7.01 (1H, s, H-8); 7.24 (2H, d, *J* = 7.8); 7.55 (2H, d, *J* = 7.8) – ArH. Found, %: C 71.14; H 5.48; N 5.01. $C_{16}H_{15}NO_3$. Calculated, %: C 71.36; H 5.61; N 5.20.

6-Amino-7-(4-bromobenzoyl)-1,4-benzodioxane (23). Yield 85%; mp 151-152°C (ethanol) [15].

6-Amino-7-(2-fluorobenzoyl)-1,4-benzodioxane (24). Yield 88%; mp 153-154°C (ethanol). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.09 (2H, m); 4.26 (2H, m) – OCH_2CH_2O; 6.30 (1H, s, H-5); 6.50 (1H, s, H-8); 7.11 (2H, br. s, NH_2); 7.31 (2H, m); 7.39 (2H, m) – ArH. Found, %: C 65.73; H 4.21; N 4.96. $C_{15}H_{12}NFO_3$. Calculated, %: C 65.93; H 4.43; N 5.13.

6-Amino-7-(3-fluorobenzoyl)-1,4-benzodioxane (25). Yield 84%; mp 124-125°C (ethanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.16 (2H, m); 4.31 (2H, m) – OCH_2CH_2O; 5.96 (2H, br. s, NH_2); 6.23 (1H, s, H-5); 6.96 (1H, s, H-8); 7.20 (1H, m); 7.31 (1H, m); 7.41 (2H, m) – ArH. Found, %: C 65.66; H 4.26; N 4.93. $C_{15}H_{12}NFO_3$. Calculated, %: C 65.93; H 4.43; N 5.13.

6-Amino-7-(methoxybenzoyl)-1,4-benzodioxane (26). Yield 77%; mp 160-161°C (ethanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 3.87 (3H, s, CH_3O); 4.17 (2H, m); 4.28 (2H, m) – OCH_2CH_2O; 5.73 (2H, br. s, NH_2); 6.23 (1H, s, H-5); 6.93 (2H, d, *J* = 7.8, H-3',5'); 7.03 (1H, s, H-8); 7.63 (2H, d, *J* = 7.8, H-2',6'). Found, %: C 67.11; H 5.14; N 4.73. $C_{16}H_{15}NO_4$. Calculated, %: C 67.36; H 5.30; N 4.91.

***o*-Acylanilides 7-18, 27-34 (General Method)**. To a solution of the corresponding *o*-aminoacylbenzene **5**, **6**, **19-26** (0.01 mol) in dioxane (30 ml) the corresponding acid chloride (10 mmol) and 3N NaOH (10 mmol) were added simultaneously in portions with stirring. Stirring was continued for 30 min and the mixture was poured into water (300 ml).

(a) The precipitated oil was extracted with CH_2Cl_2, washed with water, dried over $MgSO_4$, and, after evaporation of the solvent, the residue was recrystallized from a suitable solvent.

(b) The precipitate was filtered off, washed with water, and recrystallized.

Cyclopropyl-substituted *o*-Acylaminobenzyl Alcohols 35-46 and 58-65 (General Method). To a suspension of $NaBH_4$ (5 mmol) in ethanol (20 ml) the corresponding compound **7-18, 27-34** (5 mmol) was added with stirring, the mixture was stirred vigorously for 2-6 h until the reaction was completed (monitoring by TLC), and 10% HCl solution was added slowly until the mixture was weakly acidic. The aqueous ethanolic solution was poured into water (150 ml). The precipitate was filtered off and recrystallized from a suitable solvent. Satisfactory completion of the reduction of the *o*-acylamide **18** required heating to 40-50°C for 8 h.

Cyclization of Cyclopropyl-substituted *ortho*-Acylaminobenzyl Alcohols 35-45 and 58-65 under the Influence of Trifluoroacetic Acid (General Method). An acylaminobenzyl alcohol **35-45** or **58-65** (3 mmol) was added by portions to a solution of trifluoroacetic acid (3.5 ml) in $CHCl_3$ (10 ml) at 20°C and stirring was continued to produce a homogeneous solution (0.5-1 h); it was poured with intense stirring into a mixture of water (40 ml) and ice (40 g); carefully neutralized with saturated Na_2CO_3 solution, the organic layer was separated, the aqueous layer extracted with $CHCl_3$ (10 ml); the combined organic layers were washed with water, dried over $MgSO_4$, the solvent was evaporated and the residue was chromatographed on a column of aluminum oxide.

The yields and physicochemical characteristics of compounds **7-18**, **27-73** are cited in Table 1, their ^{1}H NMR spectra in Table 2, and their mass spectra in Table 3.

The Reaction of *o*-Acylaminobenzyl Alcohol 46 with Trifluoroacetic Acid. 4-(4-Methoxyphenoxy)-acetylamino-5-(4-hydroxybuten-1-yl)veratrole (**75**) (0.18 g, 68%) was obtained using the method above from the benzyl alcohol **46** (0.27 g). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.88 (1H, br. s, OH); 2.41 (2H, m, $C\underline{H}_2$–CH=CH); 3.71 (2H, t, *J* = 7.2, $C\underline{H}_2OH$); 3.81 (3H, s, CH_3O); 3.88 (3H, s, CH_3O); 3.90 (3H, s, CH_3O); 4.61 (2H, s, $C(O)C\underline{H}_2O$); 6.02 (1H, m, CH_2–C<u>H</u>=CH); 6.35 (1H, d, *J* = 18, CH_2–CH=C<u>H</u>); 6.87 (1H, s, H-6); 6.89 (2H, d, *J* = 8.6); 6.93 (2H, d, *J* = 8.6) – ArH, 7.39 (1H, s, H-3); 8.28 (1H, br. s, NH). Found, %: C 64.81; H 6.27; N 3.41. $C_{21}H_{25}NO_6$. Calculated, %: C 65.10; H 6.50; N 3.61.

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