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4H-3,1-BENZOXAZINES FROM BENZYL CYCLOPROPANES. FIRST EXAMPLE OF ACID CATALYZED REARRANGEMENT IN *ortho*-SUBSTITUTED BENZYLCYCLO-PROPANES

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The synthesis of 2-N-acylamino-substituted benzylcyclopropanes has been carried out. It was established that under the action of acids 2-N-acylamino-substituted benzylcyclopropanes are rearranged into the corresponding 4H-3,1-benzoxazines and not into the expected 3,1-benzoxazepines. It was shown that a similar type of rearrangement is also characteristic for 2-N-acylamino-substituted allylbenzenes.

Keywords: 4-alkyl-4H-3,1-benzoxazines, 6-allyl-7-amino-1,4-benzodioxane, 2-aminobenzylcyclopropanes, 2-N-acylaminoallylbenzenes, 2-N-acylaminobenzylcyclopropanes, 6-butyroyl-7-nitro-1,4-benzodioxane, 1-(2-N-*p*-methoxybenzoylamino)-4,5-ethylenedioxyphenylbutan-1-ol, 2-nitrobenzylcyclopropanes, rearrangements.

Benzylcyclopropanes belong to a little-studied class of compounds, although formally they are homologs of phenylcyclopropanes, the chemistry of which has been studied extremely thoroughly, especially in the region of synthesis of heterocyclic compounds of various classes [1-14]. In addition the available data on the chemical conversion of benzylcyclopropanes indicate that the introduction of a methylene group into phenylcyclopropane in the benzene ring–three-carbon ring bond leads to a significant difference in the behavior of the indicated cyclopropyl-containing substrates in identical reactions, although in certain cases phenyl- and benzylcyclopropanes behave in a similar manner [15-21].

In the present work the problem was set of comparing the behavior of *ortho* functionally-substituted benzylcyclopropanes with analogous phenylcyclopropanes under conditions of acid-catalyzed conversion. With this aim we synthesized a series of *o*-acylaminobenzylcyclopropanes and studied the probability of rearranging them under conditions in which the phenylcyclopropane analogs are converted into the corresponding 3,1-benzoxazines [3].

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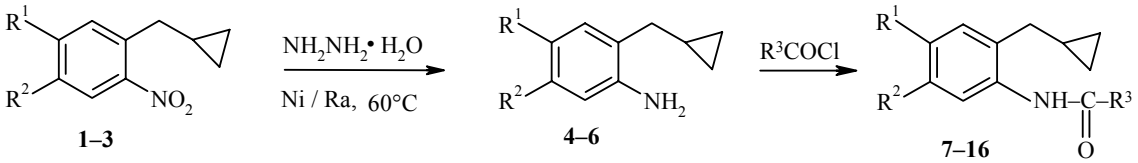
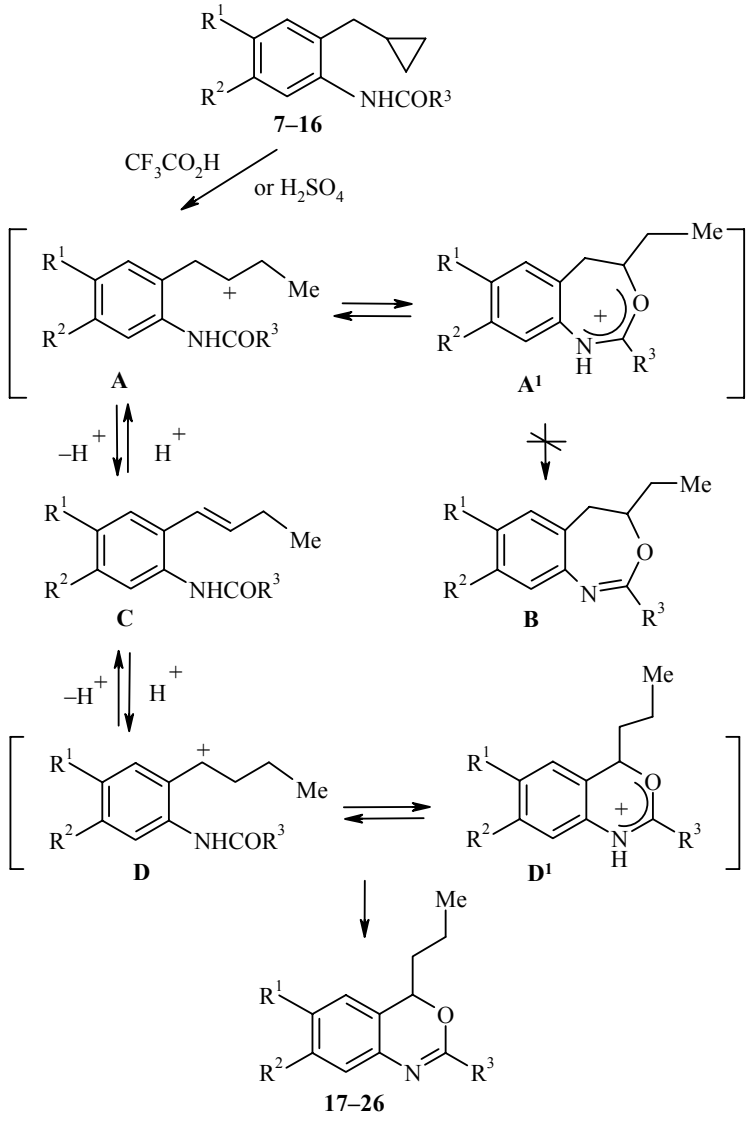
The *o*-acylaminobenzylcyclopropanes **7-16** needed for the investigation were obtained from nitro compounds **1-3** by sequential reduction and acylation.



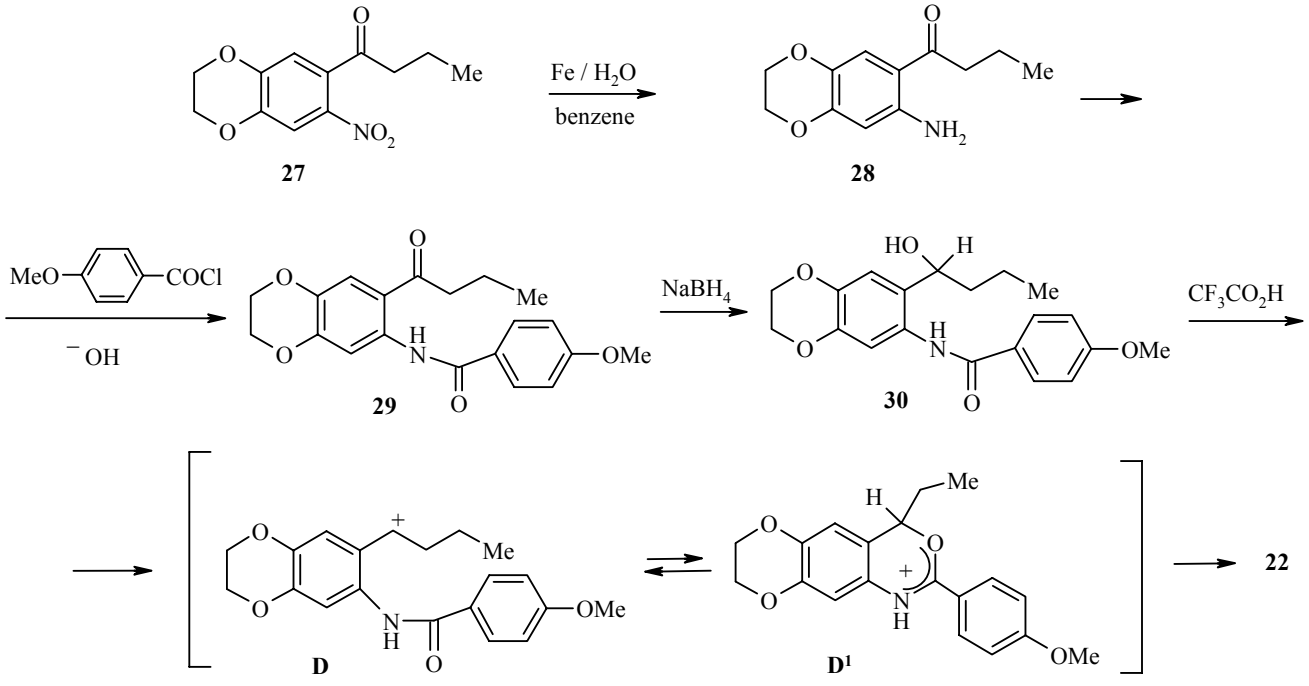
1, **4**, **7–9** $R^1 = R^2 = H$; **2**, **5**, **10–15** $R^1 = R^2 = O(CH_2)_2O$; **3**, **6**, **16** $R^1 = R^2 = OMe$;
7, 11 $R^3 = Ph$; **8, 13** $R^3 = p\text{-}MeC_6H_4$; **9, 14** $R^3 = p\text{-}BrC_6H_4$; **10** $R^3 = i\text{-}Pr$;
12, 16 $R^3 = p\text{-}MeOC_6H_4$; **15** $R^3 = p\text{-}NO_2C_6H_4$

In view of the result of converting *o*-acylaminophenylcyclopropanes and the route of carrying it out [3] in acidic media, for acylaminobenzylcyclopropanes **7-16** under the same conditions we have a right to expect the formation of heterocyclic compounds of the 3,1-benzoxazepine series (type **B**), products of the rearrangement of amides corresponding to the formation of heterocyclic ions **A** in the course of the conversion.



However it turned out that on treating *ortho*-substituted benzylcyclopropanes **7-16** with trifluoroacetic acid under standard conditions there was formed in high yield not the 4-ethyl-3,1-benzoxazepines of type **B** but the corresponding 4-propyl-3,1-benzoxazines **17-26*** (Table 2). Rearrangement of compounds **7-16** under the action of conc. H_2SO_4 at -20°C also leads to the same result.

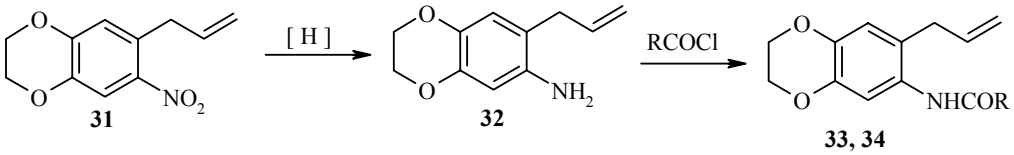
The rearrangement products, the corresponding 4-propyl-4H-3,1-benzoxazines **17-26**, may not be formed directly from 2-acylaminobenzylcyclopropanes **7-16** and, as is evident from the Scheme, are the result of secondary processes the substance of which includes the isomeric transition of ions of the homobenzyl type **A** into ions of the benzyl type **D**. It must be assumed that the cyclic 3,1-benzoxazepinium ions (type $\mathbf{A^1}$) formed in the initial stage of the rearrangement are rapidly isomerized, being thermodynamically significantly less stable, into ions of the six-membered structure $\mathbf{D^1}$. The time interval of isomerization of ions $\mathbf{A^1}$ into $\mathbf{D^1}$ is so small that we were unsuccessful in establishing the signals of protons of the cyclic ions (type $\mathbf{A^1}$) in the ^{1}H NMR spectrum. For example in a solution of 2-(4-methylbenzoyl)aminobenzylcyclopropane **8** in fluorosulfonic acid, only signals of protons belonging to the structure of the corresponding 4H-3,1-benzoxazinium ion were identified directly after mixing the reactants. It is interesting to note that a similar rapid transition of cyclic intermediates of seven-membered structure (type $\mathbf{A^1}$) into ions of a six-membered structure (type $\mathbf{D^1}$) were also observed in the acid-catalyzed reaction of *p*-nitrobenzylideneiminobenzylcyclopropane N-oxide [19]. In difference to the present case the authors of [19] successfully established by ^{1}H NMR the formation in predominant amount of cyclic ions of a seven-membered structure, which after a short time interval (~2 h) were quantitatively isomerized into ions of a six-membered structure. We propose that isomerization of ions of type $\mathbf{A^1}$ into ions of the six-membered structure $\mathbf{D^1}$ was effected through a reversible stage of forming ions of an open structure (type **A** and **D**). In view of the data of [10, 14, 19], it may be considered that the isomeric transition of ions **A** into **D** is effected through intermediate **C.**



*The meaning of R^1, R^2, and R^3 for compounds **17-26** is the same as for compounds **7-16** respectively.

Support for the proposed scheme of converting acylaminobenzylcyclopropanes **7-16** is also indicated by the alternate synthesis of 4-propyl-4H-3,1-benzoxazine (**22**) from *o*-amidophenylbutan-1-ol **30**, the compound from which under the reaction conditions the carbene ion **D** or the cyclic intermediate **D**[1] is formed directly and not indirectly as in the case of the corresponding benzylcyclopropane **12**.

We have therefore succeeded in showing for the first time that *ortho* functionally-substituted benzylcyclopropanes, although indirectly, are capable of being rearranged into stable isomeric structures.



31 **32** **33, 34**

33 R = *i*-Pr, **34** R = *p*-BrC_6H_4

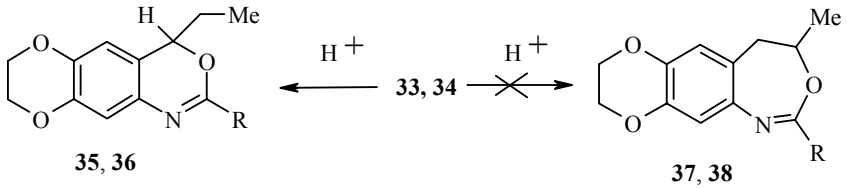
TABLE 1. Characteristics of Compounds **7-16, 29, 33, 34**

Compound	Empirical formula*	Found, % / Calculated, %			mp, °C (alcohol)	IR spectrum, ν, cm^{-1}	Yield, %
		C	H	N			
7	$C_{17}H_{17}NO$	81.14 / 81.24	6.59 / 6.86	5.32 / 5.57	118-119	3210-3340 (NH), 1640 (C=O)	94
8	$C_{18}H_{19}NO$	81.12 / 81.47	6.93 / 7.22	5.43 / 5.28	120-121	3220-3380 (NH), 1645 (C=O)	92
9	$C_{17}H_{16}NBrO$	61.23 / 61.83	4.53 / 4.88	4.19 / 4.24	147-148	3330-3460 (NH), 1650 (C=O)	89
10	$C_{16}H_{21}NO_3$	69.36 / 69.79	7.41 / 7.69	4.83 / 5.09	—	3210-3360 (NH), 1660 (C=O)	88
11	$C_{19}H_{19}NO_3$	73.49 / 73.77	5.87 / 6.19	4.38 / 4.53	—	3190-3330 (NH), 1640 (C=O)	89
12	$C_{20}H_{21}NO_4$	69.89 / 70.78	5.95 / 6.24	4.09 / 4.13	146–147	3220-3350 (NH), 1650 (C=O)	91
13	$C_{20}H_{21}NO_3$	74.39 / 74.28	6.31 / 6.55	4.09 / 4.33	—	3200-3310 (NH), 1650 (C=O)	84
14	$C_{19}H_{18}NBrO_3$	58.63 / 58.78	4.45 / 4.67	3.54 / 3.61	199–200	3220-3340 (NH), 1650 (C=O)	93
15	$C_{19}H_{18}N_2O_5$	64.13 / 64.40	4.92 / 5.12	7.56 / 7.90	—	3230-3370 (NH), 1640 (C=O)	87
16	$C_{20}H_{23}NO_4$	70.45 / 70.36	6.48 / 6.79	3.83 / 4.10	141-142	3220-3350 (NH), 1650 (C=O)	83
29	$C_{20}H_{21}NO_5$	67.31 / 67.59	5.82 / 5.96	3.79 / 3.94	201-202	—	88
33	$C_{15}H_{19}NO_3$	68.79 / 68.94	7.47 / 7.33	5.21 / 5.36	—	3210-3320 (NH), 1650 (C=O)	91
34	$C_{18}H_{16}NBrO_3$	57.63 / 57.77	3.47 / 4.31	3.53 / 3.74	—	3200-3360 (NH), 1640 (C=O)	82

*Mass spectrum, *m/z* (I_{rel}, %): compound **7** – 251 $[M]^+$ (22.1); 222 (8.2); 146 (34.8); 131 (21.9); 118 (16.9); 105 (100); 77 (62.3); 51 (7.9); compound **8** –265 $[M]^+$ (12.1); 172 (5.1); 146 (24.8); 136 (8.1); 130 (23.5); 119 (100); 91 (47.9); 77 (5.2); 65 (14.3); compound **9** –330 $[M]^+$ (11.3); 185 (100); 172 (8.1); 157 (37.9); 146 (91.5); 130 (61.8); 118 (27.1); 91 (5.1); 76 (16.2); compound **16** – 341 $[M]^+$ (29.3); 326 (5.2); 206 (33.8); 190 (24.8); 175 (7.9); 135 (100); 107 (8.1); 92 (7.3); 77 (12.1).

TABLE 2. ^{1}H NMR Spectra of Compounds **7-16, 29, 33**, and **34**

Compound	Chemical shifts, δ, ppm (*J*, Hz)
7	0.39 (2H, m, H *c*-Pr); 0.58 (2H, m, H *c*-Pr); 1.19 (1H, m, H *c*-Pr); 2.48 (2H, d, *J* = 5.4, CH_2-benzyl); 7.01 (2H, m, H arom); 7.19 (1H, t, *J* = 8.0, H arom); 7.25-7.35 (3H, m, H arom); 7.48 (2H, d, *J* = 8.0, H arom); 7.91(1H, m, H arom); 9.19 (1H, s, NH)
8	0.19 (2H, m, H *c*-Pr); 0.61 (2H, m, H *c*-Pr); 1.01 (1H, m, H *c*-Pr); 2.42 (3H, s, CH_3); 2.62 (2H, d, *J* = 4.8, CH_2-benzyl); 7.11-7.33 (5H, m, H arom); 7.76 (2H, d, *J* = 8.1, H arom); 7.91 (1H, m, H arom); 8.93 (1H, s, NH)
9	0.21 (2H, m, H *c*-Pr); 0.59 (2H, m, H *c*-Pr); 0.95 (1H, m, H *c*-Pr); 2.61 (2H, d, *J* = 5.2, CH_2-benzyl); 7.18 (1H, m, H arom); 7.23 (1H, m, H arom); 7.38 (1H, m, H arom); 7.63 (2H, d, *J* = 8.2, H arom); 7.68 (2H, d, *J* = 8.2, H arom); 7.89 (1H, m, H arom); 9.41 (1H, s, NH)
10	0.17 (2H, m, H *c*-Pr); 0.48 (2H, m, H *c*-Pr); 0.94 (1H, m, H *c*-Pr); 1.17 (6H, d, *J* = 6.4, $CH(C\underline{H}_3)_2$); 2.38 (2H, d, *J* = 5.2, CH_2-benzyl); 2.59 (1H, m, $C\underline{H}(CH_3)_2$); 4.22 (4H, m, OCH_2CH_2O); 6.78 (1H, s, H arom) and 6.82 (1H, s, H arom); 8.81 (1H, s, NH)
11	0.12 (2H, m, H *c*-Pr); 0.39 (2H, m, H *c*-Pr); 0.91 (1H, m, H *c*-Pr); 2.38 (2H, d, *J* = 5.4, CH_2-benzyl); 4.25 (4H, m, OCH_2CH_2O); 6.77 (1H, s, H arom); 6.91 (1H, s, H arom); 7.48-7.59 (3H, m, H arom); 7.95 (2H, m, H arom); 9.71 (1H, s, NH)
12	0.19 (2H, m, H *c*-Pr); 0.54 (2H, m, H *c*-Pr); 0.92 (1H, m, H *c*-Pr); 2.24 (2H, d, *J* = 5.6, CH_2-benzyl); 3.85 (3H, s, OCH_3); 4.31 (4H, m, OCH_2CH_2O); 6.91 (2H, d, *J* = 8.2, H arom); 7.06 (1H, s, H arom); 7.08 (2H, d, *J* = 8.2, H arom); 7.12 (1H, s, H arom); 9.29 (1H, s, NH)
13	0.16 (2H, m, H *c*-Pr); 0.47 (2H, m, H *c*-Pr); 0.97 (1H, m, H *c*-Pr); 2.42 (3H, s, CH_3); 2.48 (2H, d, *J* = 5.4, CH_2-benzyl); 4.26 (4H, m, OCH_2CH_2O); 6.84 (1H, m, H arom); 6.86 (1H, s, H arom); 7.25 (2H, d, *J* = 8.2, H arom); 7.86 (2H, d, *J* = 8.2, H arom); 9.17 (1H, s, NH)
14	0.12 (2H, m, H *c*-Pr); 0.41 (2H, m, H *c*-Pr); 0.91 (1H, m, H *c*-Pr); 2.44 (2H, d, *J* = 5.6, CH_2-benzyl); 4.21 (4H, m, OCH_2CH_2O); 6.81 (1H, s, H arom); 6.92 (1H, s, H arom); 7.69 (2H, d, *J* = 8.4, H arom); 7.92 (2H, d, *J* = 8.4, H arom); 9.54 (1H, s, NH)
15	0.11 (2H, m, H *c*-Pr); 0.42 (2H, m, H *c*-Pr); 0.87 (1H, m, H *c*-Pr); 2.35 (2H, d, *J* = 5.6, CH_2-benzyl); 4.27 (4H, m, OCH_2CH_2O); 6.79 (1H, s, H arom); 6.93 (1H, s, H arom); 7.34 (2H, d, *J* = 8.4, H arom); 8.13 (2H, d, *J* = 8.4, H arom); 10.05 (1H, s, NH)
16	0.21 (2H, m, H *c*-Pr); 0.56 (2H, m, H *c*-Pr); 0.93 (1H, m, H *c*-Pr); 2.14 (2H, d, *J* = 5.6, CH_2-benzyl); 3.78 (3H, s, OCH_3); 3.89 (3H, s, OCH_3); 3.97 (3H, s, OCH_3); 6.91 (2H, d, *J* = 8.0, H arom); 7.06 (1H, s, H arom); 7.08 (2H, d, *J* = 8.0, H arom); 7.12 (1H, s, H arom); 9.31 (1H, c, NH)
29	1.01 (3H, t, *J* = 7.2, $C\underline{H}_3CH_2CH_2$); 1.76 (2H, m, $CH_3C\underline{H}_2CH_2$); 2.97 (2H, t, *J* = 7.2, $CH_3CH_2C\underline{H}_2$); 3.88 (3H, c, CH_3O); 4.29 (2H, m, OCH_2CH_2O); 4.38 (2H, m, OCH_2CH_2O); 7.02 (2H, d, *J* = 8.2, H arom); 7.48 (1H, s, H arom); 7.92 (2H, d, *J* = 8.2, H arom); 8.39 (1H, s, H arom); 12.04 (1H, c, NH)
33	1.15 (6H, d, *J* = 6.2, $CH(C\underline{H}_3)_2$); 2.58 (1H, m, $C\underline{H}(CH_3)_2$); 3.22 (2H, d, *J* = 6.4, $C\underline{H}_2CH{=}CH_2$); 4.21 (4H, m, OCH_2CH_2O); 5.03 (2H, m, $C\underline{H}_2{=}CH$); 5.89 (1H, m, $CH_2C\underline{H}{=}CH_2$); 6.59 (1H, s, H arom); 6.85 (1H, s, H arom); 8.55 (1H, s, NH)
34	3.27 (2H, d, *J* = 6.4, $C\underline{H}_2CH{=}CH_2$); 4.25 (4H, m, OCH_2CH_2O); 5.11 (2H, m, $C\underline{H}_2{=}CH$); 5.88 (1H, m, $CH_2C\underline{H}{=}CH_2$); 6.65 (1H, s, H arom); 6.85 (1H, s, H arom); 7.61 (2H, d, *J* = 8.2, H arom); 7.89 (2H, d, *J* = 8.2, H arom); 9.45 (1H, s, NH)



35, **36** **37**, **38**

33, 35 R = *i*-Pr, **34, 36** R = *p*-BrC_6H_4

With the aim of clarifying whether this type of rearrangement, anomalous at first glance, is of a general character, or this special conversion applies only to acylaminobenzylcyclopropanes, we studied the reaction of alkenyl analogs of the latter, the hydrocarbon fragment of which under acid catalysis conditions is also capable of generating a carbene ion of the homobenzyl type.

The required model 2-acylaminoalkenylbenzenes **33, 34** were synthesized analogously to 2-acylaminobenzylcyclopropanes **7-16**.

It turned out that acylaminoallylbenzenes **33, 34** under the conditions used are also converted into 4H-3,1-benzoxazines **35, 36** and not into 3,1-benzoxazepines **37, 38**, i.e. it is evident that in this case the rearrangement is effected by the scheme assumed for the rearrangement of acylaminobenzylcyclopropanes **7-16**.

Consequently, unlike 2-acylaminophenylcyclopropanes directly undergoing acid-catalyzed rearrangement into 4H-3,1-benzoxazines, the 2-acylaminobenzylcyclopropanes, at least those containing no electron-withdrawing substituents in the benzene ring, are not able to be transformed under the same conditions into stable products corresponding to the direct interaction of the ion of the homobenzyl type, formed with an internal nucleophile. In spite of that, in the route of transformation of *ortho*-acylaminobenzylcyclopropanes to the final products of the reaction, the 4-propyl-4H-3,1-benzoxazines **17-26**, the cyclic ions (**A**[1]) bearing a positive charge, corresponding to the direct interaction of a carbene ion of the homobenzyl type with an internal nucleophile, are evidently formed nevertheless. The anomalous rearrangement found for 2-acylaminobenzylcyclopropanes to all appearances may be extended not only to the corresponding allylbenzenes, but also to *ortho*-substituted benzenes, which contain substituents displaying nucleophilic properties and substituents capable under the reaction conditions of generating a carbene center of the homobenzyl type.

TABLE 3. Characteristics of 4-Alkyl-4H-3,1-benzoxazines **17-26, 35, 36***

Compound	Empirical formula	Found, % / Calculated, %			Yield, %
		C	H	N	
17*[2]	$C_{17}H_{17}NO$	81.07 / 81.24	7.12 / 6.82	5.33 / 5.57	69
18	$C_{18}H_{19}NO$	81.13 / 81.48	6.97 / 7.22	5.07 / 5.28	76
19	$C_{17}H_{16}BrNO$	61.53 / 61.83	4.61 / 4.88	3.98 / 4.24	72
20	$C_{16}H_{21}NO_3$	69.43 / 69.79	7.42 / 7.69	4.81 / 5.09	63
21	$C_{19}H_{19}NO_3$	73.48 / 73.77	5.92 / 6.19	4.21 / 4.53	67
22	$C_{20}H_{21}N_4O_4$	70.47 / 70.78	6.11 / 6.24	3.89 / 4.13	65
23	$C_{20}H_{21}NO_3$	74.45 / 74.28	6.21 / 6.55	4.12 / 4.33	72
24	$C_{19}H_{18}BrNO_3$	58.91 / 58.78	4.32 / 4.67	3.39 / 3.61	71
25	$C_{19}H_{18}N_2O_5$	64.19 / 64.40	4.82 / 5.12	7.51 / 7.91	57
26	$C_{20}H_{23}NO_4$	70.11 / 70.36	6.53 / 6.79	4.41 / 4.10	76
35	$C_{15}H_{19}NO_3$	68.51 / 68.94	7.59 / 7.33	5.51 / 5.36	65
36	$C_{18}H_{16}BrNO_3$	57.52 / 57.77	4.18 / 4.31	3.49 / 3.74	79

* Compounds **17, 19-26, 35, 36** were viscous oils. Compound **18** had mp 115°C (alcohol).

*[2] Mass spectrum, *m/z* (I_{rel}, %): compound **17**, 251 [M] (21.9); 208 (100); 152 (10.1); 105 (12.3), 77 (22.4); 51 (8.3).

TABLE 4. ^{1}H NMR Spectra of Compounds **17-26, 35, 36**

Compound	Chemical shifts, δ, ppm (*J*, Hz)
17	0.95 (3H, t, *J* = 6.2, C<u>H</u>$_3$CH$_2$CH$_2$); 1.52 (2H, m, CH$_3$C<u>H</u>$_2$CH$_2$); 1.82 (2H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 5.56 (1H, m, H-4 benzoxazine); 7.12-7.65 (7H, m, H arom); 8.07 (2H, d, *J* = 8.0, H arom)
18	1.04 (3H, t, *J* = 6.6, C<u>H</u>$_3$CH$_2$CH$_2$); 1.62 (2H, m, CH$_3$C<u>H</u>$_2$CH$_2$); 1.95 (2H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 2.45 (3H, s, CH$_3$); 5.47 (1H, t, *J* = 6.5, H-4 benzoxazine); 7.17 (3H, m, H arom); 7.28 (3H, m, H arom); 7.94 (2H, d, *J* = 8.0, H arom)
19	1.05 (3H, t, *J* = 6.4, C<u>H</u>$_3$CH$_2$CH$_2$); 1.57 (2H, m, CH$_3$C<u>H</u>$_2$CH$_2$); 1.89 (2H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 5.65 (1H, m, H-4 benzoxazine); 7.21-7.43 (4H, m, H arom); 7.79 (2H, d, *J* = 8.2, H arom); 8.09 (2H, d, *J* = 8.2, H arom)
20	0.94 (3H, t, *J* = 6.2, C<u>H</u>$_3$CH$_2$CH$_2$); 1.21 (6H, d, *J* = 6.4, (C<u>H</u>$_3$)$_2$CH); 1.45 (2H, m, CH$_3$C<u>H</u>$_2$CH$_2$); 1.65 (2H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 2.55 (1H, m, (CH$_3$)$_2$C<u>H</u>); 4.21 (4H, m, OCH$_2$CH$_2$O); 5.10 (1H, m, H-4 benzoxazine); 6.38 (1H, s, H arom); 6.65 (1H, s, H arom)
21	0.96 (3H, t, *J* = 6.4, C<u>H</u>$_3$CH$_2$CH$_2$); 1.57 (2H, m, CH$_3$C<u>H</u>$_2$CH$_2$); 1.77 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 1.89 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 4.24 (4H, m, OCH$_2$CH$_2$O); 5.31 (1H, m, H-4 benzoxazine); 6.48 (1H, s, H arom); 6.82 (1H, s, H arom); 7.30–7.46 (3H, m, H arom); 8.08 (2H, d, *J* = 8.0, H arom)
22	1.02 (3H, t, *J* = 6.4, C<u>H</u>$_3$CH$_2$CH$_2$); 1.62 (2H, m, CH$_3$C<u>H</u>$_2$CH$_2$); 1.78 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 1.91 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 3.85 (3H, s, CH$_3$O); 4.24 (4H, m, OCH$_2$CH$_2$O); 5.28 (1H, m, H-4 benzoxazine); 6.51 (1H, s, H arom); 6.81 (1H, s, H arom); 6.93 (2H, d, *J* = 8.2, H arom); 8.06 (2H, d, *J* = 8.2, H arom)
23	1.02 (3H, t, *J* = 6.2, C<u>H</u>$_3$CH$_2$CH$_2$); 1.58 (2H, m, CH$_3$C<u>H</u>$_2$CH$_2$); 1.78 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 1.94 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 2.46 (3H, s, CH$_3$); 4.26 (4H, m, OCH$_2$CH$_2$O); 5.34 (1H, m, H-4 benzoxazine); 6.25 (1H, s, H arom); 6.82 (1H, s, H arom); 7.22 (2H, d, *J* = 7.8, H arom); 8.02 (2H, d, *J* = 7.8, H arom)
24	0.97 (3H, t, *J* = 6.4, C<u>H</u>$_3$CH$_2$CH$_2$); 1.52 (2H, m, CH$_3$C<u>H</u>$_2$CH$_2$); 1.76 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 1.88 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 4.24 (4H, m, OCH$_2$CH$_2$O); 5.24 (1H, m, H-4 benzoxazine); 6.49 (1H, s, H arom); 6.78 (1H, s, H arom); 7.51 (2H, d, *J* = 8.2, H arom); 7.92 (2H, d, *J* = 8.2, H arom)
25	0.91 (3H, t, *J* = 6.2, C<u>H</u>$_3$CH$_2$CH$_2$); 1. 49 (2H, m, CH$_3$C<u>H</u>$_2$CH$_2$); 1.77 (2H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 4.22 (4H, m, OCH$_2$CH$_2$O); 5.52 (1H, m, H-4 benzoxazine); 6.71 (1H, s, H arom); 6.75 (1H, s, H arom); 8.12 (2H, d, *J* = 8.4, H arom); 8.31 (2H, d, *J* = 8.4, H arom)
26	1.02 (3H, t, *J* = 6.2, C<u>H</u>$_3$CH$_2$CH$_2$); 1.62 (2H, m, CH$_3$C<u>H</u>$_2$CH$_2$); 1.77 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 1.92 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$); 3.79 (3H, s, CH$_3$O); 3.85 (3H, s, CH$_3$O); 3.94 (3H, s, CH$_3$O); 5.28 (1H, m, H-4 benzoxazine); 6.51 (1H, s, H arom); 6.80 (1H, s, H arom); 6.93 (2H, d, *J* = 8.1, H arom); 8.06 (2H, d, *J* = 8.1, H arom)
35	0.97 (3H, t, *J* = 6.3, C<u>H</u>$_3$CH$_2$); 1.21 (6H, d, *J* = 6.4, CH(C<u>H</u>$_3$)$_2$); 1.76 (2H, m, CH$_3$C<u>H</u>$_2$); 2.56 (1H, m, C<u>H</u>(CH$_3$)$_2$); 4.19 (4H, m, OCH$_2$CH$_2$O); 5.05 (1H, m, H-4 benzoxazine); 6.37 (1H, s, H arom); 6.65 (1H, s, H arom)
36	1.04 (3H, t, *J* = 6.6, C<u>H</u>$_3$CH$_2$); 1.85 (2H, m, CH$_3$C<u>H</u>$_2$); 4.22 (4H, s, OCH$_2$CH$_2$O); 5.23 (1H, m, H-4 benzoxazine); 6.45 (1H, s, H arom); 6.78 (1H, s, H arom); 7.51 (2H, d, *J* = 8.2, H arom); 7.96 (2H, d, *J* = 8.2, H arom)

EXPERIMENTAL

The ^{1}H NMR spectra were obtained on Varian VXR-400 (400 MHz) and Bruker DRX-500 (500 MHz) spectrometers in $CDCl_3$, the residual protons of the deuterated solvent acted as standard. The IR spectra were recorded on a UR-20 spectrometer in nujol and hexachlorobutadiene. The mass spectra were obtained on a Finnigan SSQ-7000 instrument, GC-MS type using a capillary column (30 m, DV-1 stationary phase, carrier gas helium) and temperature programing from 50 to 300°C (10 deg/min). Ionization energy was 70 eV. A check on the purity of the obtained compounds was carried out on Silufol plates and on Al_2O_3 of Brockmann grade II activity in the system ether–chloroform–petroleum ether (40-70°C), 1:1:3. Preparative separation of reaction mixtures was carried out on plates of Al_2O_3 of Brockmann grade II activity in the system benzene–ethyl acetate, 5:1.

2-Nitrobenzylcyclopropane (1) was obtained by the nitration of benzylcyclopropane as described in [15], yield 37.5%; bp 106-107°C (3 mm Hg), n^{20}_D 1.5447 [15].

4,5-Ethylenedioxy-2-nitrobenzylcyclopropane (2) was obtained analogously from 3,4-ethylenedioxybenzylcyclopropane, (bp 144-146°C (14 mm Hg), n^{20}_D 1.5503), yield 83%; mp 87-88°C (alcohol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.21 (2H, m, H *c*-Pr); 0.49 (2H, m, H *c*-Pr); 1.01 (1H, m, H *c*-Pr); 2.71 (2H, d, *J* = 7.6, CH_2 benzyl); 4.46 (4H, m, OCH_2CH_2O); 7.08 (1H, s, H arom); 7.53 (1H, s, H arom). Found, %: C 61.01; H 5.41; N 5.71. $C_{12}H_{13}NO_4$. Calculated, %: C 61.27; H 5.57; N 5.95.

4,5-Dimethoxy-2-nitrobenzylcyclopropane (3) was obtained by the nitration of 3,4-dimethoxybenzylcyclopropane (bp 162-164°C (19 mm Hg), n^{20}_D 1.5354) as described in [15], yield 72%; mp 75-76°C (alcohol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.24 (2H, m, H *c*-Pr); 0.56 (2H, m, H *c*-Pr); 1.11 (1H, m, H *c*-Pr); 2.89 (2H, d, *J* = 6.8, CH_2 benzyl); 3.92 (3H, s, CH_3O); 3.99 (3H, s, CH_3O); 6.98 (1H, s, H arom); 7.62 (1H, s, H arom). Found, %: C 60.46; H 6.21; N 5.71. $C_{12}H_{15}NO_4$. Calculated, %: C 60.75; H 6.37; N 5.90.

6-Butyroyl-7-nitro-1,4-benzodioxane (27) was synthesized analogously from 6-butyroyl-1,4-benzodioxane, yield 78%; mp 90-91°C (alcohol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.99 (3H, t, *J* = 7.3, $C\underline{H}_3CH_2CH_2$); 1.76 (2H, m, $CH_3C\underline{H}_2CH_2$); 2.68 (2H, t, *J* = 7.3, $CH_3CH_2C\underline{H}_2$); 4.35 (4H, m, OCH_2CH_2O); 6.80 (1H, s, H arom); 7.66 (1H, s, H arom). Found, %: C 57.12; H 5.03; N 5.31. $C_{12}H_{13}NO_5$. Calculated, %: C 57.37; H 5.21; N 5.57.

6-Allyl-7-nitro-1,4-benzodioxane (31) was obtained by the nitration of 6-allyl-1,4-benzodioxane under the action of N_2O_4, as described in [22]. Yield 71%; mp 40-41°C (alcohol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.59 (2H, d, *J* = 7.6, $C\underline{H}_2CH{=}CH_2$); 4.33 (4H, m, OCH_2CH_2O); 5.06 (2H, m, $CH_2CH{=}C\underline{H}_2$); 5.91 (1H, m, $CH_2C\underline{H}{=}CH_2$); 6.88 (1H, s, H arom); 7.52 (1H, s, H arom). Found, %: C 59.41; H 4.88; N 6.12. $C_{11}H_{11}NO_4$. Calculated, %: C 59.72; H 5.01; N 6.33.

2-Aminobenzylcyclopropane (4). Raney nickel (2 g, 33 mmol) and hydrazine hydrate (3.2 g, 100 mmol) were added in portions to a solution of 2-nitrobenzylcyclopropane (**1**) (5.3 g, 30 mmol) in ethanol (30 ml). The reaction mixture was stirred for 1 h at 20°C, poured into water (150 ml), extracted with ether (2×50 ml), and the extract dried over $MgSO_4$. After evaporating the solvent the residue was chromatographed on a column of Al_2O_3. Compound **4** (3.8 g, 86%) was obtained as a viscous oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.19 (2H, m, H *c*-Pr); 0.58 (2H, m, H *c*-Pr); 1.02 (1H, m, H *c*-Pr); 2.42 (2H, m, CH_2 benzyl); 3.52 (2H, br. s, NH_2); 6.68 (1H, dd, J_o = 8.0, J_m = 1.8, H arom); 6.75 (1H, m, H arom); 7.04 (1H, m, H arom); 7.21 (1H, dd, J_o = 8.0, J_m = 1.8, H arom). Found, %: C 81.38; H 8.67; N 9.31. $C_{10}H_{13}N$. Calculated, %: C 81.59; H 8.90; N 9.51.

2-Amino-4,5-ethylenedioxybenzylcyclopropane (5) was obtained analogously, yield 76%, viscous oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.18 (2H, m, H *c*-Pr); 0.59 (2H, m, H *c*-Pr), and 0.98 (1H, m, H *c*-Pr); 2.38 (2H, m, *J* = 7.6, CH_2 benzyl); 3.28 (2H, br. s, NH_2); 4.21 (4H, m, OCH_2CH_2O); 6.22 (1H, s, H arom); 6.73 (1H, s, H arom). Found, %: C 69.91; H 7.22; N 6.62. $C_{12}H_{15}NO_2$. Calculated, %: C 70.22; H 7.37; N 6.82.

2-Amino-4,5-dimethoxybenzylcyclopropane (6) was obtained analogously by the reduction of nitro compound **3**, yield 72%, viscous oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.17 (2H, m, H *c*-Pr); 0.56 (2H, m, H *c*-Pr); 0.97 (1H, m, H *c*-Pr); 2.43 (2H, m, CH_2 benzyl); 3.42 (2H. br. s, NH_2); 3.81 (3H, s, CH_3O); 3.83 (3H, s, CH_3O); 6.28 (1H, s, H arom); 6.78 (1H, s, H arom). Found, %: C 69.32; H 8.07; N 6.38. $C_{12}H_{17}NO_2$. Calculated, %: C 69.54; H 8.26; N 6.76.

6-Amino-7-butyroyl-1,4-benzodioxane (28) was obtained from 1,4-benzodioxane **27** by the procedure described in [23]. Yield 81%; mp 65-66°C (alcohol). ^{1}H NMR spectrum, δ, ppm, (*J*, Hz): 1.01 (3H, t, *J* = 6.8, $C\underline{H}_3CH_2CH_2$); 1.71 (2H, m, $CH_3C\underline{H}_2CH_2$); 2.79 (2H, t, *J* = 6.8, $CH_3CH_2C\underline{H}_2$); 4.17 (2H, m, OCH_2CH_2O); 4.27 (2H, m, OCH_2CH_2O); 5.86 (2H, br. s, NH_2); 6.09 (1H, s, H arom); 7.21 (1H, s, H arom). Found, %: C 64.78; H 6.69; N 6.12. $C_{12}H_{15}NO_3$. Calculated, %: C 65.14; H 6.83; N 6.33.

6-Allyl-7-amino-1,4-benzodioxane (32). Disodium disulfinate (12.2 g) and Na_2CO_3 (7.3 g) were added gradually to a suspension of nitro compound **31** (4.4 g, 20 mmol) in aqueous ethanol (1:1, 100 ml). The reaction

mixture was stirred for 1 h at 20°C, diluted with water, extracted with $CHCl_3$ (3×40 ml), and the extract dried over $MgSO_4$. The solvent was evaporated and the residue chromatographed on a column of Al_2O_3. Amino compound **32** (2.14 g, 56%) was obtained as a viscous oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.14 (2H, d, *J* = 7.2, C<u>H</u>$_2$CH=CH$_2$); 3.38 (2H, br. s, NH$_2$); 4.14 (4H, m, OCH$_2$CH$_2$O); 5.06 (2H, m, C<u>H</u>$_2$=CHCH$_2$); 5.89 (1H, m, CH$_2$=C<u>H</u>CH$_2$); 6.17 (1H, s, H arom); 7.42 (1H, s, H arom). Found, %: C 68.87; H 6.71; N 7.18. $C_{11}H_{13}NO_2$. Calculated, %: C 69.09; H 6.85; N 7.32.

2-N-Acylaminobenzylcyclopropanes 7-16, 6-N-(*p*-Methoxybenzoylamino)-7-butyroyl-1,4-benzodioxane (29), and 2-N-Acylaminoallylbenzenes 33, 34 (Tables 1 and 2) were obtained by the acylation of amino compounds **4-6, 28, 32** with acid chlorides of the appropriate acids as described in [24].

1-[2-N-(4-Methoxybenzoylamino)-4,5-ethylenedioxy]phenylbutan-1-ol (30) was obtained by the reduction of *o*-acylaminobutyrophenone **29** with $NaBH_4$ as described in [20], yield 78%; mp 150-151°C (aqueous alcohol 1:1 mixture). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.88 (3H, t, *J* = 6.8, C<u>H</u>$_3$CH$_2$CH$_2$CH$_2$); 1.26 (1H, m, CH$_3$C<u>H</u>$_2$CH$_2$CH); 1.43 (1H, m, CH$_3$C<u>H</u>$_2$CH$_2$CH); 1.74 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$CH); 1.85 (1H, m, CH$_3$CH$_2$C<u>H</u>$_2$CH); 3.37 (1H, br. s, OH); 3.83 (3H, s, CH$_3$O); 4.19 (4H, m, OCH$_2$CH$_2$O); 4.66 (1H, t, *J* = 6.6, C<u>H</u>OH); 6.56 (1H, s, H arom); 6.92 (2H, d, *J* = 8.2, H arom); 7.85 (2H, d, *J* = 8.2, H arom); 7.88 (1H, s, H arom); 9.85 (1H, s, NH). Found, %: C 66.93; H 6.22; N 3.71. $C_{20}H_{23}NO_5$. Calculated, %: C 67.21; H 6.49; N 3.92.

Isomerization of N-Acylaminobenzylcyclopropanes 7-16 and N-Acylaminoallylbenzenes 33, 34 under the Action of Trifluoroacetic Acid (General Method). The appropriate amidobenzylcyclopropane **7-16** or the corresponding amidoallylbenzene **33, 34** (2 mmol) was added gradually to trifluoroacetic acid (6 ml). After 15-30 min the temperature of the reaction mixture was raised to 30-33°C. The reaction mixture was cooled to 20°C, poured into a mixture of water (30 ml) and ice (30 g) and carefully neutralized with NaOH. The reaction products were extracted with $CHCl_3$ (3×30 ml), the extract dried over $MgSO_4$, and the solvent evaporated. The residue was chromatographed on plates of Al_2O_3 (eluent was benzene–ethyl acetate, 5:1). Yields and physicochemical characteristics of the products of isomerization are given in Tables 3 and 4.

Isomerization of 2-Benzoylamino-4,5-ethylenedioxybenzylcyclopropane (11) under the Action of Conc. H_2SO_4. Amide **11** (0.62 g, 2 mmol) was added gradually with stirring to conc. H_2SO_4 (5 ml) cooled to -20°C. The reaction mixture was stirred for 1 h at -20°C, poured into a mixture of ice (50 g) and water (50 ml), neutralized with NaOH, and the isomerization product isolated as described above. 2-Phenyl-4-propyl-4H-3,1-benzoxazine (**21**) (0.43 g, 69%) was obtained as a viscous oil. The ^{1}H NMR spectrum was identical to that of a sample obtained by isomerization of amide **11** by the action of trifluoroacetic acid.

Reverse Synthesis of 6,7-Ethylenedioxy-2-(4-methoxyphenyl)-4-propyl-4H-3,1-benzoxazine (22) from Amidoarylpropan-1-ol 30. 3,1-Benzoxazine **22** (0.48 g, 71%) was obtained from alcohol **30** (0.71 g, 2 mmol) by the procedure for isomerizing acylaminobenzylcyclopropanes **7-16**. The ^{1}H NMR spectrum of compound **22** obtained by this method was identical to the spectrum of 3,1-benzoxazine **22** obtained from the corresponding acylaminobenzylcyclopropane **12**.

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