SYNTHESIS AND BIOLOGICAL ACTIVITY OF ADAMANTANE DERIVATIVES

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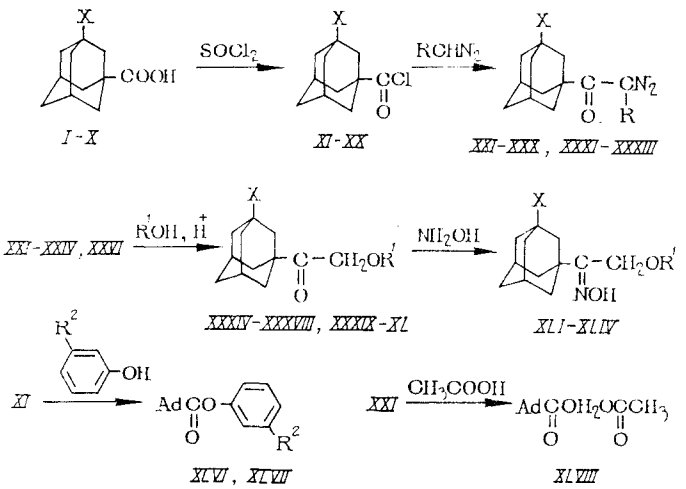
We have earlier detected anticonvulsant activity (ACA) in adamantane derivatives [1-3]. The literature also mentions the bacteriological activity of adamantanecarboxylic acids [4]. We have now synthesized a series of 3-substituted adamantanecarboxylic acids, their acid chlorides, α-diazo ketones, α-hydroxy- and α-alkoxymethyl adamantyl ketones, α-hydroxy ketone oximes, and esters to make a further study of the biological activity of adamantane derivatives.

We synthesized adamantanecarboxylic acids (I)-(X) by the published procedures [5-8]. Reaction with thionyl chloride easily formed the acid chlorides (XI)-(XX). We should note that the 3-iodo and nitrooxy groups, in contrast to bromo [9], are readily substituted by chlorine. C-Acylation of diazomethane and diazoethane with adamantanecarboxylic acid chlorides gave high yields of the yields of the α-diazo ketones (XXI)-(XXXIII), decomposition of which in aqueous and alcoholic solution in the presence of catalytic amounts of mineral acids generated the α-hydroxy- and α-alkoxymethyl adamantyl ketones (XXXIV)-(XL). Methyl 3-iodo-1-adamantanecarboxylate (XLV) was formed in quantitative yield from acid (IV) and diazomethane. We prepared phenyl 1-adamantanecarboxylates (XLVI)-(XLVII) by reaction of the phenols with 1-adamantanecarbonyl chloride (XI) and synthesized 2-acetoxy-1-(1-adamantyl)-1-ethanone (XLVIII) by refluxing 1-adamantoyldiazomethane (XXI) in acetic acid.



I-XXX: X = H, Cl, Br, I, F, C_6H_5, p-$CH_3C_6H_4$, m,p-$(CH_3)_2C_6H_3$, NO_2, ONO_2;
XXXI-XXXIII: X = H, Cl, Br, R = CH_3; XXXIV-XXXVIII: X = H, Cl, Br, I, C_6H_5, R' = H; XXXIX-XL: X = Cl, Br, R' = C_2H_5; XLI-XLIV: X = H, Cl, Br, I, R' = H; XLVI, XLVII: R^2 = H, CH_3

We verified the structures of the synthetic compounds by elemental analysis (Table 1) and IR and PMR spectroscopy. The IR spectra of α-diazo ketones (XXI)-(XXX) have the diazo

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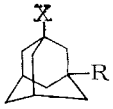
TABLE 1. Adamantane Derivatives 

Compound	X	R	Yield, %	Melting point, °C	Found, %				Formula	Calculated, %			
					C	H	N	Hal		C	H	N	Hal
XIV	I	COCl	86	76—8	40,60	4,30	—	11,00	$C_{11}H_{14}ClIO$	40,69	4,31	—	10,93
XV	F	COCl	93	31—2	60,59	6,41	—	16,20	$C_{11}H_{14}ClFO$	61,03	6,46	—	16,37
XVI	C_6H_5	COCl	81	23—5	74,20	6,84	—	12,88	$C_{17}H_{19}ClO$	74,33	6,92	—	12,91
XVII	$p-CH_3C_6H_4$	COCl	85	68—70	74,92	7,25	—	12,32	$C_{18}H_{21}ClO$	74,88	7,28	—	12,28
XVIII	$m, p-(CH_3)_2C_6H_3$	COCl	82	66—8	75,15	7,60	—	11,53	$C_{19}H_{23}ClO$	75,38	7,60	—	11,72
XIX	NO_2	COCl	92	59—61	54,01	5,71	5,70	14,25	$C_{11}H_{14}ClNO_3$	54,22	5,75	5,75	14,56
XX	ONO_2	COCl	91	65—6,5	50,90	5,38	5,40	13,59	$C_{11}H_{14}ClNO_4$	50,88	5,39	5,39	13,67
XXIV	I	$COCHN_2$	97	90—1	43,60	4,52	8,50	—	$C_{12}H_{15}IN_2O$	43,67	4,54	8,48	—
XXV	F	$COCHN_2$	95	64—5,5	65,00	6,73	12,77	—	$C_{12}H_{15}FN_2O$	64,88	6,75	12,60	—
XXVI	C_6H_5	$COCHN_2$	92	61—2,5	77,05	9,25	12,98	—	$C_{18}H_{20}N_2O$	77,15	9,25	12,95	—
XXVII	$p-CH_3C_6H_4$	$COCHN_2$	94	85—7	77,50	7,47	9,58	—	$C_{19}H_{22}N_2O$	77,56	7,48	9,52	—
XXVIII	$m, p-(CH_3)_2C_6H_3$	$COCHN_2$	95	105—7	77,88	7,80	9,12	—	$C_{20}H_{24}N_2O$	77,93	7,78	9,08	—
XXIX	NO_2	$COCHN_2$	97	125—7	57,86	6,05	16,80	—	$C_{12}H_{15}N_3O_3$	57,85	6,02	16,86	—
XXX	ONO_2	$COCHN_2$	94	72—4	54,38	5,60	15,96	—	$C_{12}H_{15}N_3O_4$	54,36	5,66	15,84	—
XXXI	H	$COC(CH_3)N_2$	78	68—70	71,29	8,27	13,01	—	$C_{13}H_{18}N_2O$	71,57	8,25	12,83	—
XXXII	Cl	$COC(CH_3)N_2$	80	109—10*	61,79	6,72	10,92	13,94	$C_{13}H_{17}ClN_2O$	61,81	6,73	11,08	14,03
XXXIII	Br	$COC(CH_3)N_2$	81	98—9*	52,52	5,73	9,50	26,85	$C_{13}H_{17}BrN_2O$	52,56	5,72	9,42	26,90
XXXIV	H	$COCH_2OH$	80	41—3	74,80	8,81	—	—	$C_{12}H_{17}O_2$	74,62	8,80	—	—
XXXV	Cl	$COCH_2OH$	89	75—6,5	63,00	7,45	—	15,53	$C_{12}H_{17}ClO_2$	63,05	7,43	—	15,51
XXXVI	Br	$COCH_2OH$	95	88—9,5	52,80	6,20	—	29,30	$C_{12}H_{17}BrO_2$	52,70	6,22	—	29,27
XXXVII	I	$COCH_2OH$	90	86—8	45,05	5,30	—	40,00	$C_{12}H_{17}IO_2$	45,03	5,31	—	39,65
XXXVIII	C_6H_5	$COCH_2OH$	84	71—2,5	79,83	8,05	—	—	$C_{18}H_{22}O_2$	80,01	8,14	—	—
XXXIX	Cl	$COCH_2OC_2H_5$	90	59—61	65,50	8,15	—	13,76	$C_{14}H_{21}ClO_2$	65,53	8,18	—	13,81
XL	Br	$COCH_2OC_2H_5$	87	65—7	55,80	6,96	—	26,42	$C_{14}H_{21}BrO_2$	55,85	6,97	—	26,54
XLI	H	$C(NOH)CH_2OH$	89	127—9	68,75	9,00	6,68	—	$C_{12}H_{19}NO_2$	68,92	9,08	6,69	—
XLII	Cl	$C(NOH)CH_2OH$	95	142—3	59,44	7,60	5,73	—	$C_{12}H_{18}ClNO_2$	59,17	7,39	5,75	—
XLIII	Br	$C(NOH)CH_2OH$	90	146—8	50,00	7,40	4,86	—	$C_{12}H_{18}BrNO_2$	50,03	7,39	4,86	—
XLIV	I	$C(NOH)CH_2OH$	91	154—5	42,95	5,36	4,15	—	$C_{12}H_{18}INO_2$	43,00	5,37	4,17	—
XLV	I	$COOCH_3$	95	37—9	45,00	5,28	—	39,50	$C_{12}H_{17}IO_2$	45,03	5,30	—	39,65
XLVI	H	$COOC_6H_5$	87	38—40	—	—	—	—	—	—	—	—	—
XLVII	H	$m-COOC_6H_4CH_3$	85	64—6	79,66	8,16	—	—	$C_{18}H_{22}O_2$	80,01	8,14	—	—
XLVIII	H	$COCH_2OCOCH_3$	85	57—9	71,00	8,41	—	—	$C_{14}H_{20}O_2$	71,20	8,47	—	—

*Melting with decomposition.

and carbonyl bands in the 2130-2115 and 1640-1620 cm^{-1} regions. The introduction of an electron-donating methyl group into the α-position to the diazo group reduces the multiplicity of the N≡N= and C=N bonds in diazo ketones (XXXI)-(XXXIII) and reduces the frequency of the IR bands to 2018-2075 cm^{-1} (N≡N) and 1625 cm^{-1}(C=O). In the reaction products of the α-diazo ketones, (XXXIV)-(XL), the diazo bands are replaced by the bands of the relevant functional group and of the nonconjugated carbonyl group at 3460-3500 cm^{-1} (OH), 1710-1690 cm^{-1} (C=O), and 1240 cm^{-1} (C—O—C). In compounds (XLI)-(XLIV) the carbonyl band is replaced by a broad band in the 3300-3200 cm^{-1} region (NOH). The PMR spectra contain the signals of the CH group at 5.35-5.55 ppm in compounds (XXI)-(XXX), the CH_3 group at 1.95-3.71 ppm in compounds (XXVII), (XXVIII), (XXXI)-(XXXIII), (XLV), (XLVII), and (XLVIII), and the phenyl group at 7.05-7.28 ppm in compounds (XXXVI)-(XXXVIII), (XXXVIII), (XLVI), and (XLVII).

EXPERIMENTAL PHARMACOLOGY

We used mice of both sexes of weight 18-22 g for the pharmacological studies. Compounds were administered intraperitoneally in 2% starch slurry. We examined compounds (II), (IV)-(X), and (XXXIV)-(XLVIII) in comparison with hexamidine. The experimental figures were processed statistically by Litchfield and Wilcoxon's method with P = 0.05 [10].

We examined the acute toxicity [11], the ACA, by the maximal electroshock (MES) test [12] and the corazole test, and the antitremor activity, by the nicotine and arecoline tests [13], evaluating the doses protecting half the animals from convulsion (ED_{50}). The depressant and stimulant effects were determined visually. We examined the effect on motor coordination (neurotoxic effect) by the rotating rod procedure, evaluating TD_{50}, the dose causing half the mice to fall off the rod in a 3-min period [14]. For the active compounds we calculated the conventional pharmacological margin of the effect (CPM) — the ratio of LD_{50} to ED_{50} in the MES test. The antimicrobial activity toward *Staphylococcus aureus* and *Escherichia coli* was assayed by the serial dilution technique. The bacterial loading of the working solution was 250,000 microbial bodies per ml. As the effective dose we took the lowest concentration that inhibited the growth of the bacterial cultures [11]. The results of these tests are summarized in Table 2.

We have already detected ACA in 1-adamantanecarboxylic acid (I), whose ED_{50} is 300 mg per kg. Introduction into position 3 of the admantane ring of acid (I) of chlorine, bromine, iodine, fluorine, or of the nitro or nitrooxy substituents removes the ACA of compounds (II)-(V), (IX), and (X). The phenyl group enhances the ACA of acid (VI) by a factor of 2.5 relative to (I) — ED_{50} is 135 mg/kg; the peak of the effect is apparent 5 min after administration against 60 min with (I) and lasts for 2 h. The presence of one methyl group in the phenyl substituent reduces the ACA to ED_{50} 395 mg/kg in acid (VII) and delays to 30 min the appearance of the peak, while the presence of two methyl groups eliminates the ACA in acid (VIII).

The acids found to be active in the MES test have no effect on corazole and nicotine convulsions in doses equal to ED_{50}, implying that they have no n-cholinolytic effect.

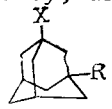
Methyl and Phenyl adamantanecarboxylates (XLV)-(XLVII) have no anticonvulsant effect.

Replacement of the carboxyl group of the acids by hydroxymethylcarbonyl or ethoxymethylcarbonyl enhances the ACA of compounds (XXXIV)-(XXXIX). Ethoxy ketones (XXXIX) and (XL) are less active than the equivalent hydroxy ketones. Hydroxy ketone (XXXV) is most active in the MES tes (ED_{50} 108 mg/kg). The activity of the iodo-substituted hydroxy ketone (XXXVII) is slightly lower (ED_{50} 120 mg/kg), whereas its activity in the corazole test is very high (ED_{50} 110 mg/kg). The ACA of compounds (XXXV) and (XXXVII) may equal that of hexamidine, since the difference in the ACA is statistically insignificant. Their acute toxicity is 2.3 times lower than that of hexamidine and consequently their CPM is double that of hexamidine. These compounds are also active in the corazole test; the peak of their effect is apparent after 5 min, whereas that of hexamidine appears after 4 h.

Screening of the hydroxy ketones (XXXI)-(XXXVIII) for antitremor activity by the arecoline and nicotine tests in doses equal to ED_{50} in the MES test revealed that compound (XXXIV) intensifies tremor in the arecoline test, compound (XXXVI) shortens the duration of tremor in the arecoline test while reducing tremor in 50% of the animals in the nicotine test, and compound (XXXVII) slightly attenuates the tremor in both tests.

Oximation of the hydroxy ketones reduces the ACA in compounds (XLI)-(XLIV).

TABLE 2. Anticonvulsant Activity, Acute Toxicity, and Antimicrobial Activity of Adamantane Derivatives



Compound	X	R	ACA, ED_{50}, mg/kg		Acute toxicity, LD_{50}, mg/kg	Conventional pharmacological margin, LD_{50}/ED_{50}		Antimicrobial activity, μg/ml	
			MES test	corazole test		corazole test	MES test	E. coli	S. aureus
I*	H	COOH	300 (256—351)	170	600	—	—	500	500
II	Cl	COOH	Inactive	Inactive	1500	—	—	250	62,5
III	Br	COOH	"	—	600	—	—	—	—
IV	I	COOH	"	Inactive	1500	—		Ineffective	62,5
V	F	COOH	"	"	1500	—	—	500	250
VI	C_6H_5	COOH	135 (112—163)	"	588 (518—668)	4,3	—	1000	250
VII	p- $CH_3C_6H_4$	COOH	395 (341—458)	"	610 (485—750)	1,5	—	—	—
VIII*	m,p- $(CH_3)_2C_6H_3$	COOH	Inactive	"	1500	—	—	—	—
IX	NO_2	COOH	"	"	950 (909—993)	—	—	500	125
X	ONO_2	COOH	"	"	950 (909—992)	—	—	250	250
XXXIV	H	$COCH_2OH$	190 (186—192)	210 (172—256)	600 (541—666)	3,1	2,8	500	500
XXXV	Cl	$COCH_2OH$	108 (80—146)	170 (128—226)	795 (729—867)	7,3	4,6	500	500
XXXVI	Br	$COCH_2OH$	187 (144—243)	129 (119—149)	700 (642—763)	3,7	5,4	1000	1000
XXXVII	I	$COCH_2OH$	120 (89—162)	110 (90—134)	798 (731—871)	6,6	7,2	15,6	31,25
XXXVIII	C_6H_5	$COCH_2OH$	190 (178—210)	Inactive	680 (610—763)	3,5	—	Ineffective	
XXXIX	Cl	$COCH_2OC_2H_5$	250 (210—360)	123 (109—139)	600 (531—635)	2,4	4,8	500	31,25
XL	Br	$COCH_2OC_2H_5$	Inactive	Inactive	740 (661—829)	—	—	Ineffective	31,25
XLI	H	$C(NOH)CH_2OH$	250 (214—311)	230 (193—274)	780 (740—860)	3,1	3,4	500	500
XLII	Cl	$C(NOH)CH_2OH$	200 (178—230)	175 (135—228)	650 (571—680)	3,2	3,7	1000	500
XLIII	Br	$C(NOH)CH_2OH$	Inactive	Inactive	500 (435—575)	—	—	500	1000
XLIV	I	$C(NOH)CH_2OH$	430 (347-533)	330 (239—455)	1500	—	—	500	31,25
XLV	I	$COOCH_3$	Inactive	Inactive	"	—	—	125	31,25
XLVI	H	$COOC_6H_5$	"	"	1330 (1031—1716)	—	—	125	125
XLVII	H	m-$COOC_6H_4CH_3$	"	"	1500	—	—	250	31,25
XLVIII	H	$COCH_2OCOCH_3$	"	"	1500	—	—	1000	500
Hexamidine	—	—	90 (79—103)	70 (58—84)	340 (288—401)	3,8	4,8	—	—

*The bacteriostatic activity has been described earlier [4]. The ACA of compound (III) was described earlier [1]; brackets enclose the limits of variation.

We examined the dynamics of the development of the anticonvulsant effect of compounds (XXXIV)-(XLIV). The peak ACA appears after 5 min. Compound (XXXV) shows the most rapid fall in ACA; after 15 min its ED_{50} is already 150 mg/kg. The same effect is apparent in (XXXIV).

These 3-substituted adamantane derivatives are moderately or slightly toxic substances (LD_{50} from 500 to 1500 mg/kg and more); they are 1.5-4 times less than hexamidine. Administration in the toxic doses (300 mg/kg and above) causes loss of motor coordination and depression of the central nervous system. A stimulant effect at these doses is apparent only in (XXXIV).

When examined by the rotating rod method, acid (VI) has a marked neurotoxic effect 5 min after administration; it lasts for 1 h (TD_{50} 125 mg/kg, protective index LD_{50}/TD_{50} 4.7). In acid (VII) the peak of the neurotoxic effect is apparent after 30 min and lasts 2 h (TD_{50} 290 mg/kg, protective index 2.1).

The bacteriostatic activity of these 1,3-disubstituted adamantane derivatives toward *S. aureus* and *E. coli* varies from 15.6 to 1000 μg/ml. Hydroxyketone (XXXVII) is most active, suppressing the growth of *S. aureus* in a concentration of 31.3 μg/ml and that of *E. coli* in a concentration of 15.6 μg/ml.

These tests suggest that anticonvulsant and antibacterial compounds could profitably be sought among adamantane derivatives.

EXPERIMENTAL CHEMISTRY

Spectra were recorded on: IR: a UR-20 in carbon tetrachloride; PMR: an RS-60 high-resolution spectrometer in carbon tetrachloride.

The acid chlorides, except for (XIV), (XVIII), and (XX), were prepared by reaction with thionyl chloride in the presence of catalytic amounts of DMF by the usual procedure.

3-Iodo-1-adamantanecarbonyl Chloride (XIV). A solution of acid (IV) (3.06 g, 0.01 mole) [6] in dry ether (50 ml) was refluxed for 4 h with thionyl chloride (1.45 ml, 0.02 mole) and DMF (1-2 drops). The solvent was removed under vacuum and the residue was recrystallized from hexane to give (XIV) (2.7 g, 86%).

Compounds (XVIII) and (XX) were prepared in the same way.

Adamantanoyldiazomethanes (XXI)-(XXX). These were prepared by the Arndt—Eistert method [15].

Adamantanoyldiazoethanes (XXXI)-(XXXIII). An ethereal solution of the acid chloride (0.01 mole) was added dropwise with stirring and cooling to −5°C to an ethereal solution of diazoethane (0.015 mole) [16] and triethylamine (0.01 mole). After the addition the solution was stirred for 3-4 h. Cold water was added to dissolve the triethylamine salt. The ethereal layer was separated, washed with water, and dried, and the ether was removed. The residue of the diazo ketone was recrystallized from hexane or cyclohexane.

2-Hydroxy-1-adamantyl-1-ethanone (XXXIV). To a solution of diazo ketone (XXI) (2 g, 0.01 mole) [17] in dioxane (30 ml) were added water (20 ml) and 5% perchloric acid (1 ml). The mixture was heated on a water bath for several hours until the evolution of nitrogen ceased and the solution was colorless. The solvent was removed under aspirator vacuum, leaving an oil that crystallized on standing. The crystals were pressed and recrystallized from hexane—ether (5:1) to give (XXXIV) (1.5 g, 80%). Compounds (XXXV)-(XXXVIII) were prepared in the same way.

2-Ethoxy-1-(3-chloro-1-adamantyl)-1-ethanone (XXXIX). To a solution of (XXII) (2.38 g, 0.01 mole) [2] in alcohol (40 ml) was added 5% perchloric acid (2 ml). The mixture was refluxed until the solution was colorless. The solvent was removed and the residue was pressed to give (XXXIX) (1.82 g, 72%). Compound (XL) was prepared from (XXIII) [2] in the same way.

2-Hydroxy-1-adamantyl-1-ethanone Oxime (XLI). A mixture of (XXXIV) (1.94 g, 0.01 mole), hydroxylamine hydrochloride (2.5 g, 0.015 mole), pyridine (5 ml), and methyl alcohol (40 ml) was heated on a water bath for 2.5 h. The solution was cooled and poured into water (50 ml); the resulting precipitate was filtered off and recrystallized from cyclohexane—ether (4:1) to give (XLI) (1.7 g, 89%).

Compounds (XLII)-(XLIV) were prepared in the same way.

Methyl 3-Iodo-1-adamantanecarboxylate (XLV). This was prepared from acid (IV) and diazomethane by the standard procedure [18].

Phenyl 1-Adamantanecarboxylate (XLVI). Acid chloride (XI) (1.98 g, 0.01 mole) [19] was mixed with phenol (0.94 g, 0.01 mole); after the reaction the oil was left for several hours to crystallize and then recrystallized from aqueous methanol to give (XLVI) (2.2 g, 87%) (literature mp 37-38°C [20]).

m-Methylphenyl 1-Adamantanecarboxylate (XLVII). A mixture of acid chloride (XI) (1.98 g, 0.01 mole) and m-cresol (1.5 g) was warmed at 30-50°C for 30 min and then dissolved in chloroform, washed with water, and evaporated. The residue was recrystallized from methanol to give (XLVII) (2.2 g, 85%).

2-Acetoxy-1-(1-adamantyl)-1-ethanone (XLVIII). A solution of (XXI) (2.04 g, 0.01 mole) in acetic acid (40 ml) was refluxed until the solution was colorless. Some of the acid was removed and the residue was poured into cold water. The resulting precipitate was filtered off and recrystallized from hexane to give (XLVIII) (1.95 g, 84%).

LITERATURE CITED

1. A. L. Fridman, V. S. Zalesov, I. K. Moiseev, et al., Khim. Farm. Zh., No. 7, 6 (1974).
2. A. L. Fridman, V. S. Zalesov, L. O. Kon'shina, et al., Khim. Farm. Zh., No. 4, 35 (1976).
3. A. L. Fridman, V. S. Zalesov, N. A. Kolobov, et al., Khim. Farm. Zh., No. 11, 29 (1974).
4. G. I. Danilenko, G. K. Palii, N. A. Mokhort, et al., in: Physiologically Active Substances [in Russian], Vol. 7, Kiev (1975), pp. 144-147.
5. H. Stetter and K. Wulff, Chem. Ber., 95, 2302 (1962).
6. H. Stetter and I. Mayer, Chem. Ber., 95, 2302 (1962).
7. G. I. Danilenko, V. I. Votyakov, O. T. Andreeva, et al., Khim. Farm. Zh., No. 6, 37 (1976).
8. M. L. Bagal and V. I. Lantvoev, Zh. Org. Khim., 9, 291 (1973).
9. A. L. Fridman, N. A. Kolobov, and S. A. Petukhov, Zh. Org. Khim., 11, 660 (1975).
10. M. L. Belen'kii, Elements of the Quantitative Evaluation of Pharmacological Effect [in Russian], Riga (1959), pp. 71-92.
11. G. N. Pershin: in: Methods of Experimental Chemotherapy [in Russian], Moscow (1959), pp. 109-117, 456-460.
12. K. S. Raevskii, Farmakol. Toksikol., No. 4, 495 (1961).
13. V. S. Zalesov, Farmakol. Toksikol., No. 4, 418 (1963).
14. N. W. Dunham and T. S. Miya, J. Am. Pharm. Assoc., Sci. Ed., 46, 208 (1957).
15. W. E. Bachmann and W. S. Struve, in: Org. React., 1, 53 (1948).
16. B. Eistert, M. Regitz, G. Heck, et al., Methoden zur Herstellung und Umwandlung von aliphatischen Diazoverbindungen, Stuttgart (1968), p. 539.
17. S. Tadashi, E. Shogi, and T. Takeshi, Bull. Chem. Soc. Jpn., 42, 1617 (1969).
18. K. Weigand and G. Hilgetag, Experimental Methods in Organic Chemistry [Russian translation], Moscow (1969), p. 394.
19. F. U. Schollkopf, Angew. Chem., 72, 147 (1960).
20. B. I. No, Yu. V. Popov, and S. S. Novikov, Inventor's Certificate No. 467896; Otkrytiya, No. 15, 41 (1975).