addition of water, 170 mg. (97%) of crude product, m.p. 192–194°, was obtained. Recrystallization from water gave needles, m.p. 194–195°. The pyrimidine VI traveled as a single spot on paper, R_f 0.67, solvent system A. Paper chromatography of the mother liquors showed the same spot only, thus indicating that the isomeric 2-amino-4-chloro-5-fluoropyrimidine was not formed in the reaction. The ultraviolet and infrared spectra were similar to those found by Duschinsky.[4a]

Anal. Calcd. for $C_4H_3ClFN_3$: C, 32.52; H, 2.05; Cl, 24.04; N, 28.49. Found: C, 32.46; H, 1.98; Cl, 24.28; N, 28.38.

2,4-Diamino-5-fluoropyrimidine (VII).—A mixture of 80 mg. (0.54 mmole) of VI, 5 ml. 5% ethanolic ammonia, and 200 mg. of ammonium chloride was heated at 140° for 19 hr. in a Parr bomb. The mixture was filtered, evaporated to dryness *in vacuo*, dissolved in 2 ml. of water, and brought to pH 12 with 0.2 ml. of 10% NaOH. This solution was evaporated to dryness *in vacuo*, and the desired product was separated by sublimation at 20 mm. and 140°, yielding 25 mg. (36%) of VII (m.p. 156–157° with partial recrystallization, remelting at 161–161.5°). Resublimation raised the m.p. to 164–165° with partial recrystallization, remelting at 166.5–167°; $\lambda_{max}^{pH\ 7\ buffer}$ 289 mμ (log ε 3.77); λ_{max}^{Nujol} 2.98, 3.15, 6.00, 6.23, 6.59, 6.71, 6.95, 8.25, 10.13, 10.65, 10.73, 12.90 μ.

Anal. Calcd. for $C_4H_3FN_4$: C, 37.51; H, 3.93; F, 14.83., Found: C, 37.65; H, 4.01; F, 15.11.

2-Chloro-4-ethoxy-5-fluoropyrimidine (VIII).—To a solution of 775 mg. (4.64 mmoles) of 2,4-dichloro-5-fluoropyrimidine (I) in absolute ethanol was added 2.9 ml. of 1.6 *N* ethanolic sodium ethoxide. The mixture was evaporated to 3 ml. and 7 ml. of water was added. An oil formed which solidified on cooling; this solid was removed by filtration, giving 800 mg. (96%) of product, m.p. 31–32°; purification by sublimation raised this to m.p. 35–36°; λ_{max}^{water} 261.5 mμ (log ε 3.72); λ_{max}^{film} 3.40, 6.35, 6.78, 6.90, 7.14, 7.45, 8.05, 8.21, 8.68, 9.80, 10.32, 10.50, 11.45, 12.45, 13.05 μ.

Anal. Calcd. for $C_5H_6ClFN_2O$: C, 40.80; H, 3.43; Cl, 20.05; F, 10.76. Found: C, 40.76; H, 3.40; Cl, 19.98; F, 10.52.

2-Chloro-5-fluoro-4-hydroxypyrimidine (IX).—A mixture of 1.96 g. (11.7 mmoles) of I and 6.2 ml. (11.8 mmoles) of 1.9 *N* NaOH was warmed to 45° and stirred for 45 min. at the end of which time the mixture was neutral. An additional 6.2 ml. of 1.9 *N* NaOH was added, and the mixture was stirred until the oil dissolved, requiring 15 min. After cooling, 1 ml. of concentrated HCl was added, causing the immediate precipitation of 1.38 g. of product, m.p. 170–171°. An additional 0.1 g. (same as above by infrared spectrum) was recovered from the filtrate giving a total yield of 85%. Evaporation of the mother liquors *in vacuo* gave a solid material whose infrared spectrum was similar to the pure product. Paper chromatography gave single identical spots for the pure compound and the residue in the mother liquor; solvent system A, R_f 0.76, for pure compound and residue; solvent system B, R_f 0.93, for pure compound and residue. Recrystallization from absolute ethanol, prolonged heating being avoided, raised the melting point to 176–177° with partial recrystallization and remelting at 228–243°; $\lambda_{max}^{0.1\ N\ CHl}$ 229 mμ (log ε 3.72), 258–259 mμ (log ε 3.70); λ_{max}^{Nujol} 6.09, 6.28, 6.48, 6.65, 7.75, 8.00, 8.60, 10.39, 10.90, 12.78, 14.55 μ. The material is the same as that prepared and characterized by Duschinsky.[8]

Anal. Calcd. for $C_4H_2ClFN_2O$: C, 32.34; H, 1.36; F, 12.80. Found: C, 32.35; H, 1.42; F, 14.64.

Acknowledgment.—The author wishes to express his gratitude and thanks to Dr. R. Duschinsky of Hoffman-La Roche, Inc., Nutley, N. J.

New 1-Aminomethylbenzocyclobutenes

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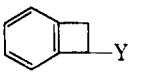
In view of the chemical uniqueness of a four-membered ring fused to an aromatic nucleus and the similarity of this system to the phenethyl chain, several amines containing the 1-benzocyclobutenyl group were synthesized for pharmacological evaluation. Until recently,[1] only two such compounds, 1-aminobenzocyclobutene[2] and N,N-dimethyl-1-aminomethyl-2-phenylbenzocyclobutene,[3] were known. In addition to the first amine, we have prepared four new 1-aminomethylbenzocyclobutenes and a related morpholine derivative.

1-Cyanobenzocyclobutene[4] (Ia), obtained by the benzyne-mediated cyclization of *o*-chlorohydrocinnamonitrile,[5] was hydrolyzed to benzocyclobutene-1-carboxylic acid (Ib). Treatment of the corresponding acid chloride Ic with sodium azide in toluene provided 1-aminobenzocyclobutene (Table I, III) in 40% yield. The direct conversion of the acid Ib to the amine III with hydrazoic acid[2] proceeded in somewhat higher yield.



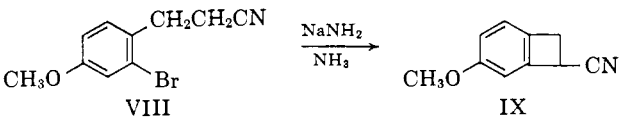
Ia, Y = CN
b, Y = CO_2H
c, Y = COCl

IIa, Y = $CH_2NHCOCH_3$
b, Y = CH_2OTs

1-Aminomethylbenzocyclobutene (IV) was prepared both by hydrolysis of the amide IIa from reductive acylation of 1-cyanobenzocyclobutene (Ia) and by lithium aluminum hydride reduction of the nitrile Ia.

The tosylate IIb of 1-hydroxymethylbenzocyclobutene was obtained with some modifications by the method of Cava and Mitchell[6]; aminolysis of this material with methylamine, dimethylamine, and morpholine provided compounds V, VI, and VII, respectively. As reported for the reaction of 1-hydroxymethyl-2-phenylbenzocyclobutene tosylate with dimethylamine,[3] the tosyl group of IIb is displaced without any apparent ring enlargement.[7] In order to substantiate the assigned structures, N,N-dimethyl-1-aminomethylbenzocyclobutene maleate (VI) was synthesized independently by reductive alkylation of 1-aminomethylbenzocyclobutene (IV) and was found to be identical by melting point and spectral comparison with the product obtained from the tosylate IIb.

Alkylation of ethyl cyanoacetate with 2-bromo-4-methoxybenzyl chloride, followed by hydrolysis of the resulting cyano ester and decarboxylation of the intermediate cyano acid, provided 2-bromo-4-methoxyhydrocinnamonitrile (VIII). Treatment of VIII with



VIII IX

sodamide in liquid ammonia afforded 1-cyano-5-methoxybenzocyclobutene (IX) in a 55% yield.

(1) After completion of this work, reports of amino- and aminoalkyl-substituted benzocyclobutenes appeared in the patent literature: (a) K. Ley, H. Walz, and W. Redetzky, Belgian Patent 630,171 (1963); (b) C. Kaiser and C. L. Zirkle, U. S. Patent 3,149,159 (1964); (c) Ciba S. A., French Patent 1,369,046 (1964).

(2) L. Horner, W. Kirmse, and K. Muth, *Chem. Ber.*, **91**, 430 (1958).

(3) A. T. Blomquist and C. G. Bottomley, *Ann.*, **653**, 67 (1962).

(4) M. P. Cava, R. L. Litle, and D. R. Napier, *J. Am. Chem. Soc.*, **80**, 2257 (1958).

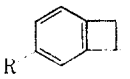
(5) J. F. Bunnett and J. A. Skorcz, *J. Org. Chem.*, **27**, 3836 (1962).

(6) M. P. Cava and M. J. Mitchell, *ibid.*, **27**, 631 (1962).

(7) The quantitative conversion of 1-hydroxymethylindane tosylate to a 2-hydroxytetralin ester during formolysis has been noted by R. Huisgen G. Seidl, and I. Wimmer, *Tetrahedron*, **20**, 623 (1964).

TABLE I

AMINE DERIVATIVES OF 1-BENZOCYCLOBUTENE

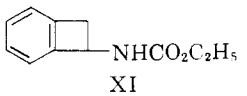


No.	R	n	Am	M.p., °C.[a]	Formula	Calcd., % Cl	Calcd., % N	Found, % Cl	Found, % N
III	H	0	$NH_2 \cdot HCl$	185.5–187	$C_8H_{10}ClN$	22.78	9.00	22.84	9.00
IV	H	1	$NH_2 \cdot HCl$	214–216	$C_9H_{12}ClN$	20.89	8.26	21.02	8.32
V	H	1	$NHCH_3 \cdot HCl$	193–195	$C_{10}H_{14}ClN$	19.30	7.63	19.37	7.59
VI	H	1	$N(CH_3)_2 \cdot$ maleate	117–119.5	$C_{15}H_{19}NO_4$	*b*	5.05	*b*	5.05
VII	H	1		216–216.5	$C_{13}H_{18}ClNO$	14.79	5.84	14.66	5.81
X	OCH_3	1	$NH_2 \cdot HCl$	163–164	$C_{10}H_{14}ClNO$	17.75[c]	7.02	17.98	7.15

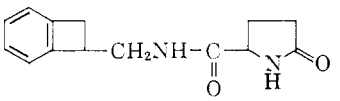
[a] Compounds III and IV were recrystallized from ethanol–ether and the other four from 2-propanol. [b] *Anal.* Calcd.: C, 64.97; H, 6.90. Found: C, 65.17; H, 6.94. [c] *Anal.* Calcd.: C, 60.10; H, 7.06. Found: C, 59.97; H, 7.25.

1-Aminomethyl-5-methoxybenzocyclobutene (X) was formed by reduction of the bicyclic nitrile IX.

The carbamate XI and the amide XII, prepared from the amines III and IV, respectively, were also evaluated biologically.



XI



XII

With few exceptions, the described benzocyclobutene derivatives were of little biological interest. Several of the amines in Table I exhibited evidence of analgetic activity as measured in mice by the hot plate method.[8,9] On a milligram basis, IV displayed analgetic action equivalent to that of morphine, but with a somewhat more rapid rate of onset and of appreciably shorter duration. None of the other amines was of comparable potency.

Experimental[10]

1-Cyanobenzocyclobutene (Ia) was prepared from *o*-chlorohydrocinnamonitrile by the method of Bunnett and Skorcz.[5] In a typical experiment the chloronitrile (0.12 mole) was allowed to react with potassium amide (0.41 mole) in 1.2 l. of liquid ammonia for 30 min.; distillation afforded 10.2 g. (66%) of product, b.p. 66–67° (0.2 mm.) [lit.[4] b.p. 88° (1.3 mm.)].

Benzocyclobutene-1-carboxylic acid (Ib) was obtained in yields ranging from 70 to 90% by the alkaline hydrolysis of nitrile Ia as outlined by Cava and Mitchell.[6]

Benzocyclobutene-1-carbonyl Chloride (Ic).—A solution of benzocyclobutene-1-carboxylic acid (53 g., 0.36 mole) in 45 ml. of thionyl chloride was stirred at 25° for 2 hr., then heated gently for 30 min. The excess reagent was removed under vacuum, and the residual liquid was distilled to yield 55.8 g. (93%) of the acid chloride, b.p. 103° (12 mm.).

Anal. Calcd. for C_9H_7ClO: C, 64.88; H, 4.24; Cl, 21.28. Found: C, 65.28; H, 4.34; Cl, 20.83.

1-Aminobenzocyclobutene Hydrochloride (III).—A solution of benzocyclobutene-1-carbonyl chloride (12 g., 0.072 mole) in 50 ml. of dry toluene was added to 9.75 g. (0.25 mole) of sodium azide in toluene (50 ml.), and the mixture was refluxed for 17 hr. The solid was filtered, and the filtrate was refluxed with 75 ml. of concentrated HCl. After 7 hr. the aqueous layer was separated and evaporated to dryness. Recrystallization of the residual solid afforded 4.8 g. (40%) of the amine salt as pale tan plates.

The reaction of 74.1 g. (0.5 mole) of benzocyclobutene-1-carboxylic acid (Ib) and 0.9 mole of sodium azide in a mixture of chloroform and concentrated H_2SO_4 by the procedure of Horner and co-workers[7] gave 40.5 g. (56%) of the amine hydrochloride III.

1-Aminomethylbenzocyclobutene Hydrochloride (IV).—A mixture of 1-cyanobenzocyclobutene (12.9 g., 0.1 mole) and 0.15 g. of platinum oxide in 50 ml. of acetic anhydride was treated with hydrogen at 25° and an initial pressure of 3.3 atm. for 32 hr. The catalyst was removed, and the filtrate was poured into 300 ml. of ice water, which then was saturated with $NaHCO_3$. The organic layer was taken up in 300 ml. of ether, which was dried (K_2CO_3) and evaporated. Distillation of the residual oil afforded 11.2 g. (64%) of **N-acetyl-1-aminomethylbenzocyclobutene (IIa)** as a colorless, viscous liquid, b.p. 150–154° (0.5 mm.).

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.39; H, 7.47; N, 7.99. Found: C, 75.52; H, 7.83; N, 8.15.

An 11-g. (0.063-mole) portion of the amide IIa in 100 ml. of 20% HCl was refluxed for 22 hr. The solution was diluted with water, filtered, and evaporated to dryness. Recrystallization of the residue gave 7.9 g. (72%) of colorless plates.

Reduction of 0.1 mole of the nitrile Ia with 0.3 mole of $LiAlH_4$ in ether, followed by treatment with ethereal HCl, gave 13.4 g. (79%) of the amine hydrochloride IV.

1-Hydroxymethylbenzocyclobutene Tosylate (IIb).—A solution of tosyl chloride (76.2 g., 0.40 mole) in 150 ml. of pyridine was added over a 5-hr. period to a solution of 1-hydroxymethylbenzocyclobutene (46.9 g., 0.34 mole), obtained in 94% yield by the $LiAlH_4$ reduction of benzocyclobutene-1-carboxylic acid[6] (Ib), in 100 ml. of pyridine kept between 0–10°. The mixture was stirred an additional 16 hr. with cooling and then was poured into 1 l. of ice water. The separated oil was taken up in 1 l. of ether, which was washed several times with 250-ml. portions of 2 *N* H_2SO_4, once with 5% $NaHCO_3$ (300 ml.), and finally with water. Evaporation of the dried solvent gave an oil which solidified on refrigeration under Skelly B. The colorless granules weighed 88.4 g. (88%), m.p. 53–58° (lit.[6] m.p. 49–55° and 73–74°). Recrystallization from cyclohexane and from *t*-butyl alcohol failed to alter the melting point range.

Anal. Calcd. for $C_{16}H_{16}O_3S$: C, 66.64; H, 5.59; S, 11.12. Found: C, 66.77; H, 5.63; S, 10.93.

N-Methyl-1-aminomethylbenzocyclobutene Hydrochloride (V).—A solution of the tosylate IIb (17.3 g., 0.06 mole) in 125 ml. of benzene saturated at 10° with methylamine was heated in an autoclave at 100° for 24 hr. The cooled mixture was washed with dilute $NaHCO_3$ solution, then with water, and was dried (Na_2SO_4). The liquid remaining after solvent evaporation was dissolved in anhydrous ether and was treated with dry HCl. The deposited solid was recrystallized to afford 8.0 g. (73%) of white flakes.

N,N-Dimethyl-1-aminomethylbenzocyclobutene maleate (VI) was prepared from 14.4 g. (0.05 mole) of the tosylate IIb and 100 ml. of dimethylamine-saturated benzene as outlined for the monomethyl compound V. Recrystallization of the maleate provided 9.9 g. (72%) of colorless needles.

The reaction of 1-aminomethylbenzocyclobutene, liberated from 5 g. (0.03 mole) of the amine hydrochloride IV with aqueous NaOH, and a mixture of 88% formic acid (10 g.) and 37% aqueous

(8) N. B. Eddy and D. Leimbach, *J. Pharmacol. Exptl. Therap.*, **107**, 385 (1953).

(9) This observation is consistent with the reported analgetic properties of the aminoalkylbenzocyclobutenes listed in ref. 1c and of the isomeric 2-aminoindane hydrochloride [L. B. Witkin, C. F. Heubner, F. Galdi, E. O'Keefe, P. Spitaletta, and A. J. Plummer, *ibid.*, **133**, 400 (1961)].

(10) Melting points were taken with a Thomas-Hoover capillary apparatus and are corrected.

formaldehyde (8 g.) at 100° for 18 hr. gave an amine, which readily formed the maleate VI (5.05 g.) in 61% over-all yield, m.p. 117–120°. A mixture melting point with the maleate obtained from the tosylate IIb was 115–119°. Their infrared and ultraviolet spectra were identical; λ_{max}^{EtOH} 270 mμ (ε 1960), 265 (2140), 259 (1700), and 252 (1400).

N-(1-Benzocyclobutenylmethyl)morpholine Hydrochloride (VII).—A solution of the tosylate IIb (10.1 g., 0.035 mole) and 8.7 g. (0.10 mole) of morpholine in 40 ml. of toluene was refluxed for 20 hr. under nitrogen. The precipitated salt was filtered, and the filtrate was evaporated. The residual oil was taken up in ether, which was shaken with water, dried (K_2CO_3), and saturated with dry HCl. The white needles weighed 6.4 g. (76%).

2-Bromo-4-methoxybenzyl chloride was synthesized from *m*-bromoanisole (293 g., 1.57 moles), 37% aqueous formaldehyde (270 g.), and HCl gas by a published procedure.[11] The product amounted to 259 g. (70%), b.p. 127–131° (3.8 mm.), lit.[11] b.p. 107° (1 mm.).

Ethyl 2-Bromo-4-methoxybenzylcyanoacetate.—To a solution of sodium ethoxide (1.55 moles) in 1 l. of absolute ethanol was added 860 g. (7.6 moles) of ethyl cyanoacetate. The milky solution was stirred for 1 hr. and then was treated with 358 g. (1.52 moles) of 2-bromo-4-methoxybenzyl chloride over a 2-hr. period with the temperature kept near 25°. After an additional hour of stirring at 25°, the solution was refluxed overnight. The solvent was removed under vacuum, and the organic residue was taken up in 500 ml. of ether, which was dried and evaporated. Distillation of the remaining liquid gave unchanged ethyl cyanoacetate, followed by 340 g. (72%) of product, b.p. 148–151° (0.05 mm.). A portion was redistilled for analysis, b.p. 143° (0.025 mm.).

Anal. Calcd. for $C_{13}H_{14}BrNO_3$: C, 50.01; H, 4.52; N, 4.49. Found: C, 50.11; H, 4.56; N, 4.37.

2-Bromo-4-methoxybenzylcyanoacetic Acid.—The ester (322 g., 1.03 moles) was added in 15 min. to 550 ml. of 10% NaOH kept near 20° by external cooling. The solution was stirred for 20 min. and then was acidified with 150 ml. of concentrated HCl. After the addition of the acid, the resulting mixture was stirred for 1 hr. The gummy solid was filtered, washed with water, and dried to give 238 g. (81%) of crude cyano acid. An analytical sample melted at 145.5–148.5° after several recrystallizations from benzene.

Anal. Calcd. for $C_{11}H_{10}BrNO_3$: C, 46.50; H, 3.59; N, 4.93; neut. equiv., 284.12. Found: C, 46.38; H, 3.29; N, 4.98; neut. equiv., 281.14.

2-Bromo-4-methoxyhydrocinnamonitrile (VIII).—A solution of the crude cyano acid (207 g., 0.73 mole) in 400 ml. of dimethylacetamide was heated in a distillation apparatus until the vapor temperature reached 150°. At this point distillation was stopped, and the solution was refluxed for 2 hr., then cooled. After dilution with 250 ml. of water, the insoluble liquid was extracted with ether, which was dried and evaporated. Distillation of the residue afforded 159 g. (91%) of colorless liquid, b.p. 115–120° (0.15 mm.).

Anal. Calcd. for $C_{10}H_{10}BrNO$: C, 50.02; H, 4.20; N, 5.84. Found: C, 50.08; H, 4.12; N, 5.74.

1-Cyano-5-methoxybenzocyclobutene (IX).—The nitrile VIII (36 g., 0.15 mole) was allowed to react with 0.6 mole of commerical sodamide in 500 ml. of liquid ammonia for 3.5 hr. The reaction mixture was neutralized with excess ammonium nitrate, and the ammonia was allowed to evaporate. Water (150 ml.) was added to the residue, and the crude product was taken up in two 150-ml. portions of chloroform. After drying (Na_2SO_4), the solvent was removed under vacuum. Distillation of the remaining liquid provided 13.2 g. (55%) of the bicyclic nitrile, b.p. 101–105° (0.6 mm.). A redistilled sample, b.p. 93° (0.1 mm.), was used for analysis.

Anal. Calcd. for $C_{10}H_9NO$: C, 75.44; H, 5.70; N, 8.80. Found: C, 75.52; H, 5.52; N, 8.78.

1-Aminomethyl-5-methoxybenzocyclobutene hydrochloride (X) was synthesized by reduction of 9.6 g. (0.06 mole) of the nitrile IX with $LiAlH_4$ (2.88 g., 0.076 mole) in anhydrous ether. Distillation of the crude product provided 5.8 g. of a colorless liquid, b.p. 90–105° (1 mm.). An ethereal solution of the material was treated with dry HCl to afford 2.3 g. (19% over-all) of white granules.

(11) B. Lythgoe, S. Trippett, and J. C. Watkins, *J. Chem. Soc.*, 4060 (1956).

N-Carbethoxy-1-aminobenzocyclobutene (XI) was prepared by the reaction of 3 g. (0.019 mole) of the amine hydrochloride III in a solution of triethylamine (3.9 g.) and chloroform with 2.1 g. (0.019 mole) of ethyl chloroformate. The yield of white needles was 3.4 g. (94%), m.p. 76–77.5° after recrystallization from Skelly B.

Anal. Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33. Found: C, 69.27; H, 6.67; N, 7.41.

N′-(1-Benzocyclobutenylmethyl)-5-oxo-2-pyrrolidinecarboxamide (XII).—To the mixed anhydride prepared from 1.55 g. (0.012 mole) of 5-oxo-2-pyrrolidinecarboxylic acid and equivalent amounts of triethylamine and ethyl chloroformate in 50 ml. of methylene dichloride at −10° was added a mixture of amine hydrochloride IV (2 g., 0.012 mole) and triethylamine (1.2 g.) in methylene dichloride. Elution of the crude product (1.2 g.) from a column of alumina (30 g.) with chloroform–methanol (2:1) gave 0.9 g. (31%) of a white, powdery material, m.p. 103–108° after recrystallization from chloroform–Skelly B.

Anal. Calcd. for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.62. Found: C, 68.70; H, 6.89.

Acknowledgment.—The authors thank Dr. M. Finkelstein and the Lakeside Pharmacology Department for the biological data, Dr. C. I. Judd and Dr. R. C. Ursillo for helpful discussions, and Mr. F. E. Kaminski for technical assistance.

A New Group of Antifibrillants. N-(ω-Aminoalkyl)phthalimides

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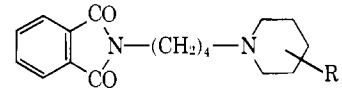
In earlier communications[1,2] the synthesis of a new group of antifibrillant N-(ω-aminoalkyl)phthalimides was reported. Of these, N-[4-(3-methylpiperidino)-butyl]phthalimide (Ia) and N-[4-(4-methylpiperidino)-butyl]phthalimide (Ib) has the highest activity. The 3-methylpiperidine compound (Ia) proved to be 1.6 times as potent in auricular and 2.5 times as potent in ventricular fibrillation as quinidine, while its toxicity was only 1.6 times higher than that of quinidine.[3]



Ia, R = 3-CH_3
b, R = 4-CH_3

In the present communication the nature of the amino group and the number of the members of the alkyl chain were varied. The synthesis of the new compounds was carried out by the following methods.

A. $o\text{-}C_6H_4(CO)_2N(CH_2)_nBr \xrightarrow{2HNR_2}$

$o\text{-}C_6H_4(CO)_2N(CH_2)_nR_2 + NR_2H_2{}^+Br^-$

(1) (a) K. Hideg and H. O. Hankovszky, *Acta Chim. Acad. Sci Hung.*, **39**, 391 (1963); (b) K. Hideg, L. Szekeres, H. O. Hankovszky, and J. Papp, 2nd International Pharmacological Meeting, Prague, August 20–23, 1963, *Biochem. Pharmacol., Suppl.*, **12**, 171 (1963).

(2) K. Hideg and H. O. Hankovszky, *Acta Chim. Acad. Sci. Hung.*, in press.

(3) L. Szekeres, K. Hideg, H. O. Hankovszky, and J. Papp, *Acta Physiol. Acad. Sci. Hung.*, in press.