solution of 2-propynyl bromide (29.7 g., 0.25 mole) in 50 ml. of anhydrous ether was added dropwise to a stirred mixture of 6.1 g. (0.25 atom) of magnesium, 0.06 g. of mercuric chloride and 100 ml. of anhydrous ether. As soon as the reaction initiated, the mixture was maintained at −5 to −10° throughout the addition. After being stirred for an additional hr. at −5°, the mixture was treated dropwise over a period of 1 hr. with a solution of ethyl 2-methyl-3-oxo-1-pyrrolidinecarboxylate (34.3 g., 0.2 mole) in 60 ml. of dry benzene, the temperature kept at 0°. To facilitate the stirring a liberal amount (about 50 ml.) of anhydrous ether was added. Stirring was continued for 15 hr. at room temperature. The Grignard complex was decomposed by pouring the mixture into 500 g. of ice containing 25 g. of ammonium chloride. The aqueous layer was separated and extracted with three 200-ml. portions of ether. The organic solution and the ethereal extracts were combined and dried over anhydrous magnesium sulfate. The residue obtained after removal of the solvents was fractionated under reduced pressure to give 21.5 g. (50%) of ethyl 3-hydroxy-2-methyl-3-(2-propynyl)-1-pyrrolidinecarboxylate as a light colored oil. Similarly prepared was ethyl 3-hydroxy-3-(2-propynyl)-1-pyrrolidinecarboxylate in a 32% yield.

E. Ethyl 3-Cyclohexyl-3-hydroxy-1-pyrrolidinecarboxylate.—A solution of 6 g. (0.025 mole) of ethyl 3-hydroxy-3-phenyl-1-pyrrolidinecarboxylate in 100 ml. of ethanol and 2 g. of 5% rhodium-on-alumina were hydrogenated at 3.5 kg./cm.^{2} pressure and at room temperature until the calculated amount of hydrogen had been absorbed. The mixture was filtered, the residue obtained after concentration of the filtrate was distilled under reduced pressure.

Acknowledgment.—The authors wish to thank Dr. John W. Kissel and his associates for the pharmacological screening of the compounds.

Pyrrolidines. VIII. 3-Acyloxy-3-Aryl-1-Ethyl- and -1-Methylpyrrolidines[1]

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The method of Kuhn and Osswald[5] for the synthesis of ethyl 3-oxo-1-pyrrolidinecarboxylates has been extended for the preparation of 1-acyl-3-pyrrolidones. Reaction of 1-acetyl-3-pyrrolidones and ethyl 3-oxopyrrolidinecarboxylates with arylmagnesium halides yielded respectively 3-aryl-1-acetyl-3-pyrrolidinols and ethyl 3-aryl-3-hydroxy-1-pyrrolidinecarboxylates, which were reduced

(1) Since the completion of this manuscript, another report covering certain 3-acyloxy-3, phenylpyrrolidines has been published [J. F. Cavalla, J. Davoll, M. J. Dean, C. S. Franklin-D. M. Temple, J. Wax, and C. V. Winder, *J. Med. Pharm. Chem.*, **4**, 1 (1961)]. As the synthetic approaches in our work were somewhat different from the published paper, we wish to report our studies in the present paper.

by means of lithium aluminum hydride to 3-aryl-1-ethyl- and -1-methyl-3-pyrrolidinols. Esterification of these tertiary alcohols produced the desired 3-acyloxy-3-aryl-1-ethyl- and -1-methylpyrrolidines for analgesic testing.

Using Dieckmann reaction and subsequent hydrolysis and decarboxylation, Ruzicka and Seidel[2] attempted to prepare 3-pyrrolidone from ethyl 2-ethoxycarbonylmethylaminopropionate. A piperidine-like smelling oil which rapidly turned to a glassy mass was obtained. By means of a similar sequence of reactions Prill and McElvain[3] succeeded in synthesizing and characterizing 1-methyl-3-pyrrolidone. This compound was described to be extremely easily oxidized even by air. Leonard and his co-workers[4] prepared 1-methyl-5-ethyl-3-pyrrolidone, which also decomposed rapidly. Seemingly the unstable nature of these pyrrolidones made them unattractive as intermediates for our synthetic studies on pyrrolidine compounds.

This difficulty was resolved when Kuhn and Osswald[5] published their paper on the synthesis of diethyl 4-oxo-1,3-pyrrolidinedicarboxylates from N-ethoxycarbonylamino acid esters and α,β-unsaturated esters in the presence of metallic sodium. After partial hydrolysis and decarboxylation, ethyl 3-oxo-1-pyrrolidinecarboxylates are formed. The amino function of these 3-pyrrolidones is masked by an ethoxycarbonyl group. Consequently they are stable compounds. In the preceding article of this series[6] we reported that this method has been employed for the preparation of twelve 3-oxo-1-pyrrolidinecarboxylates with various substituents at 2- and 5-positions of the nucleus. The carbonyl group at the 3-position has also been selectively reacted with different Grignard reagents to give 3-substituted 3-hydroxy-1-pyrrolidinecarboxylates.

We have now found that this method can be extended for the synthesis of 1-acyl-3-pyrrolidones. For instance, N-acetylalanine ethyl ester (I) was condensed with ethyl acrylate to yield ethyl 1-acetyl-5-methyl-4-oxo-3-pyrrolidinecarboxylate (II). After partial hydrolysis and decarboxylation, 1-acetyl-2-methyl-3-pyrrolidone (III) was obtained in good yield. Similar to its 1-ethoxycarbonyl analog, the 1-acetyl derivative was treated with a Grignard reagent to produce its corresponding 3-pyrrolidinol (IV).

1-Acetyl-3-aryl-3-pyrrolidinols and ethyl 3-aryl-3-hydroxy-1-pyr-

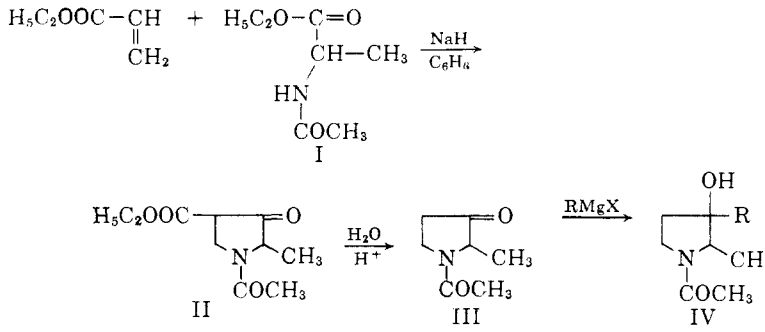
(2) L. Ruzicka and C. F. Seidel, *Helv. Chim. Acta*, **5**, 719 (1922).

(3) E. A. Prill and S. M. McElvain, *J. Am. Chem. Soc.*, **55**, 1233 (1933).

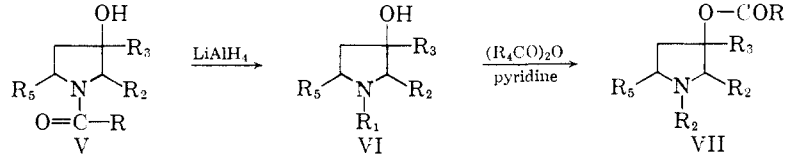
(4) N. J. Leonard, F. E. Fischer, E. Barthel, Jr., J. Figueras, Jr., and W. C. Wildman, *ibid.*, **73**, 2371 (1951).

(5) R. Kuhn and G. Osswald, *Chem. Ber.*, **89**, 1423 (1956).

(6) Pyrrolidines. VII, Y. H. Wu, W. A. Gould, W. G. Lobeck, Jr., H. R. Roth, and R. F. Feldkamp, *J. Med. Pharm. Chem.*, **5**, 752 (1962).



rolidinecarboxylates (V) thus prepared were converted respectively to 3-aryl-1-ethyl- and -1-methyl-3-pyrrolidinols (VI) by lithium aluminum hydride reduction. The formation of a methylamine from a urethane[7] and an ethylamine from an acetamide[8] by means of lithium aluminum hydride has been known. Esterification of these tertiary alcohols by the usual acid anhydride–pyridine method[9] produced the desired 3-acyloxy-3-aryl-1-ethyl- and -1-methylpyrrolidines (VII).



R = OC_2H_5 or CH_3; R_1 = CH_3 or C_2H_5; R_2 = H or CH_3; R_3 = aryl; R_4 = CH_3, C_2H_5, C_3H_7; R_5 = H or CH_3.

Pharmacology.—The 3-acyloxy-3-aryl-1-ethyl- and -1-methylpyrrolidines were tested for analgesic activity in fasted male rats by the radiant heat method. All compounds were administered orally. The most active analgesic compounds of the series were No. 2, 4, 5 and 10. The doses of these compounds which produced a 50% increase in reaction time ranged from 16 to 35 mg./kg. in comparison to 22.5 mg./kg. for codeine sulfate as the standard. The pharmacology of 1,2-dimethyl-3-phenyl-3-propionoxypyrrolidine has been extensively described.[10,11] This compound is now under clinical study.[12,13]

(7) R. L. Dannley, M. Lukin, and J. Shapiro, *J. Org. Chem.*, **20**, 92 (1955).
(8) A. Uffer and E. Schlittler, *Helv. Chim. Acta*, **31**, 1397 (1948).
(9) A. Ziering and J. Lee, *J. Org. Chem.*, **12**, 911 (1947).
(10) J. W. Kissel, J. R. Albert, and G. C. Boxill, *J. Pharmacol. Exptl. Therap.*, **134**, 332 (1961).
(11) J. R. Albert, A. G. Wheeler, H. C. Hawkins, and J. W. Kissel, *The Pharmacologist*, **3**, 264 (1961).
(12) L. J. Cass and W. S. Frederick, *Current Therapeutic Research*, **3**, 97 (1961).
(13) S. R. Splitter, *ibid.*, **3**, 472 (1961).

Experimental[14]

Ethyl 3-Aryl-3-hydroxy-1-pyrrolidinecarboxylates.—The preparation of ethyl 3-aryl-3-hydroxy-1-pyrrolidinecarboxylates has been reported.[6]

3-Aryl-1-methyl-3-pyrrolidinols and their Hydrochlorides.—A solution of ethyl 3-aryl-3-hydroxy-1-pyrrolidinecarboxylate (0.1 mole) in 150 ml. of tetrahydrofuran was added dropwise over a period of 1 hr. and with stirring to a slurry of lithium aluminum hydride (8.36 g., 0.22 mole) in 150 ml. of tetrahydrofuran. After having been refluxed for 4 hr., the mixture was cooled in an ice bath, treated carefully with 12 ml. of water, and filtered. The solid cake was extracted several times with hot ethanol. The combined filtrate and extracts were concentrated. The residue was either distilled under reduced pressure or recrystallized from isopropyl ether. The hydrochloride salt was prepared by adding an equivalent amount of anhydrous hydrogen chloride to an ethanolic solution of the free base and diluting the solution to cloudiness with anhydrous ether.

Seven 3-aryl-1-methyl-3-pyrrolidinols were prepared by this procedure. Their physical properties are listed in Table I.

Ethyl 1-Acetyl-4-oxo-3-pyrrolidinecarboxylate.—A solution of N-acetylglycine ethyl ester (370.1 g., 2.6 moles) in 660 ml. of dry benzene was added dropwise to a stirred suspension of sodium hydride (45.8% pure, 133.6 g., 2.6 moles) in 2.64 l. of dry benzene. After one quarter of the solution was added, the mixture was gently heated to initiate the reaction. Heating was discontinued once the reaction started. The rest of the solution was added at such a rate as to maintain gentle refluxing throughout the addition. The reaction mixture was stirred overnight at room temperature and treated afterwards with 255.3 g. (2.6 moles) of ethyl acrylate with stirring and dropwise over a period of 50 min. After being stirred for an additional 30 min. at room temperature and refluxed for 2 hr. thereafter, the mixture was treated with 1.01 l. of 3 *N* hydrochloric acid. The aqueous layer was separated from the benzene solution and extracted with three 200-ml. portions of chloroform. The benzene solution and the chloroform extracts were combined and concentrated. The oily residue was dissolved in 1 l. of carbon tetrachloride. On storing at 0° overnight, the solution deposited 190.6 g. of crystalline ethyl 1-acetyl-4-oxo-3-pyrrolidinecarboxylate, m.p. 55–57°. The rest of the solution was concentrated, and fractionated under reduced pressure to collect an oil, b.p. 154–164° (0.5 mm.). The distillate solidified on standing, m.p. 55–57° and amounted to 100.4 g., making the total yield 219.0 g. (57.3%) for the product.

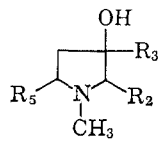
Anal. Calcd. for $C_9H_{13}NO_4$: N, 7.03. Found: N, 7.04.

1-Acetyl-3-pyrrolidone.—A mixture of 291.0 g. (1.46 moles) of ethyl 1-acetyl-4-oxo-3-pyrrolidinecarboxylate and 1.3 l. of water containing 13 ml. of concd. hydrochloric acid was refluxed for 4 hr. The resulting solution was concentrated to one fourth of its original volume and extracted with four 400-ml. portions of chloroform. The combined chloroform extracts were dried over anhydrous magnesium sulfate. The oily residue obtained after filtration and removal of the solvent was distilled under reduced pressure to obtain 77.6 g. (41.7%) of an oil, b.p. 120–123° (0.55 mm.), $n^{25}D$ 1.4978.

Anal. Calcd. for $C_6H_9NO_2$: C, 56.68; H, 7.14; N, 11.02. Found: C, 56.66; H, 7.18; N, 10.88.

(14) All melting points and boiling points are uncorrected. Microanalyses by Schwarzkopf Microanalytical Laboratories, Woodside, New York.

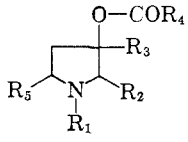
TABLE



			Yield, %[a]			M.p., °C.	
				Hydrochloride			
R_2	R_3	R_5	Base	from base	overall	Base	Hydrochloride
H	C_6H_5	H	89.0	71.8	64.9	88–98[b] (0.15 mm.)	146–148
H	C_6H_5	CH_3	78.6	92.5	72.9	67–69	199–201
CH_3	$C_6H_5CH_2$	H	59.7	71.2	42.4	85–90	161–163
CH_3	C_6H_5	H	89.5	82.5	74.0	81–83	204–206
CH_3	2-$CH_3C_6H_4$	H	70.7	85.0	60.1	91.93	199–201
CH_3	4-$CH_3OC_6H_4$	H	78.2	73.6	56.8	89–91	190–192
CH_3	3-ClC_6H_4	H	69.2	79.5	55.0	109–111	173–175

[a] Based on purified products. [b] Boiling point.

TABLE



						Yield, %[a]			Base	
							Hydrochloride		B.p.	
No.	R_1	R_2	R_3	R_4	R_5	Base	from base	overall	°C.	Mm.	$n^{25}D$
1	CH_3	H	C_6H_5	C_2H_5	H	78.2	83.3	65.0	93–96	0.2	1.5131
2	CH_3	CH_3	$C_6H_5CH_2$	C_2H_5	H	89.8	84.3	75.0	98–105	0.15	
3	CH_3	CH_3	C_6H_5	CH_3	H	69.6	81.7	56.8	66–68[b]		
4	CH_3	CH_3	C_6H_5	C_2H_5	H	92.5	83.4	77.3	106–108	0.2	1.5130
5	CH_3	CH_3	C_6H_5	n-C_3H_7	H	[c]	[c]	54.5	[c]		[c]
6	CH_3	CH_3	2-$CH_3C_6H_4$	C_2H_5	H	79.6	71.4	56.8	125–130	0.5	1.5202
7	CH_3	CH_3	4-$CH_3OC_6H_4$	C_2H_5	H	83.3	66.7	55.6	110–115	0.2	1.5198
8	CH_3	CH_3	3-ClC_6H_4	C_2H_5	H	81.8	59.3	48.4	120–125	0.35	1.5241
9	CH_3	H	C_6H_5	C_2H_5	CH_3	75.5	51.6	39.0	94–100	0.2	
10	C_2H_5	CH_3	C_6H_5	C_2H_5	H	78.4	80.4	63.0	100–106	0.15	1.5135

[a] Based on purified products. [b] Melting point. [c] The hydrochloride was prepared from the

1-Acetyl-3-phenyl-3-pyrrolidinol.—An ethereal solution of phenylmagnesium bromide (0.2 mole) in 40 ml. of anhydrous ether was added dropwise in a period of 30 min. to a solution of 1-acetyl-3-pyrrolidone (25.4 g., 0.2 mole) in 100 ml. of tetrahydrofuran. The reaction mixture was refluxed for 5.5 hr. The Grignard complex was decomposed with 50 ml. of saturated ammonium chloride solution. The mixture was extracted several times with chloroform. The chloroform extract was dried over anhydrous magnesium sulfate. The thick oily residue obtained after filtration and concentration of the chloroform solution was fractionally distilled to give 7.5 g. of a distillate with b.p. 160–169° (0.15 mm.).

I

3-ARYL-1-METHYL-3-PYRROLIDINOLS

Formula	Analyses: Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
$C_{11}H_{15}NO \cdot HCl$	61.82	62.12	7.55	7.68	16.59	16.81
$C_{12}H_{17}NO \cdot HCl$	63.29	63.07	7.96	8.11	15.57	15.70
$C_{13}H_{19}NO \cdot HCl$	64.58	64.57	8.34	8.42	14.67	14.35
$C_{12}H_{17}NO \cdot HCl$	63.29	63.34	7.96	8.28	15.57	15.62
$C_{13}H_{19}NO \cdot HCl$	64.58	64.23	8.34	8.43	14.67	14.37
$C_{13}H_{19}NO_2 \cdot HCl$	60.57	60.57	7.82	7.98	13.76	13.41
$C_{12}H_{16}ClNO \cdot HCl$	54.97	55.07	6.54	6.99	27.05	26.64

II

3-ACYLOXY-3-ARYL-1-ETHYL- AND -1-METHYLPYRROLIDINES

Hydrochloride m.p., °C.	Formula	Analyses: Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
139–140	$C_{14}H_{19}NO_2 \cdot HCl$	62.33	62.37	7.47	7.56	13.15	13.05
224–226	$C_{16}H_{23}NO_2 \cdot HCl$	64.53	64.57	8.12	8.15	11.90	11.75
192–194	$C_{14}H_{19}NO_2 \cdot HCl$	62.33	62.41	7.47	7.33	13.15	12.98
198–201	$C_{15}H_{21}NO_2 \cdot HCl$	63.48	63.62	7.81	8.07	12.49	12.38
184–186	$C_{16}H_{23}NO_2 \cdot HCl$	64.53	64.64	8.12	7.95	11.91	11.90
178–181	$C_{16}H_{23}NO_2 \cdot HCl$	64.52	64.79	8.12	7.86	11.92	11.76
151–153	$C_{16}H_{25}NO_3 \cdot HCl$	61.23	61.53	7.71	7.76	11.30	11.45
177–179	$C_{15}H_{20}ClNO_2 \cdot HCl$	56.61	56.53	6.65	6.89	22.28	22.17
142–144	$C_{15}H_{21}NO_2 \cdot HCl$	63.48	63.72	7.82	7.84	12.49	11.79
209–211	$C_{16}H_{23}NO_2 \cdot HCl$	64.52	64.71	8.12	8.20	11.91	11.70

crude base.

Pure 1-acetyl-3-phenyl-3-pyrrolidinol was obtained as a viscous oil by redistilling the crude product, b.p. 172–174° (0.1 mm.), yield 4.3 g. (10.5%).

Anal. Calcd. for $C_{12}H_{15}NO$: C, 70.22; H, 7.37; N, 6.83. Found: C, 70.10; H, 7.49; N, 6.94.

Ethyl 1-Acetyl-5-methyl-4-oxo-3-pyrrolidinecarboxylate.—A solution of N-acetylalanine ethyl ester (108.1 g., 0.67 mole) in 150 mole of dry benzene was added dropwise with stirring to a suspension of sodium hydride (51.5% pure, 31.2 g., 0.67 mole) in 1.2 l. of dry benzene. After one fourth of the solution was added, the mixture was gently heated to initiate the reaction, and then heating

was discontinued. The rest of the solution was added dropwise at a rate to maintain the gentle refluxing. The sodium salt of N-acetylalanine ethyl ester thus formed was treated dropwise with ethyl acrylate (67.6 g., 0.67 mole) over a period of 30 min. The mixture was stirred and refluxed for 1.5 hr. and allowed to cool to room temperature; 3 *N* hydrochloric acid (225 ml.) was stirred into the mixture. The benzene layer was separated and the aqueous solution was extracted several times with benzene. The combined benzene solutions were concentrated. The residue was distilled to give 89.0 g. (62.3%) of ethyl 1-acetyl-5-methyl-4-oxo-3-pyrrolidinecarboxylate as a colorless oil, b.p. 105–107° (0.15 mm.), $n^{25}D$ 1.4830.

Anal. Calcd. for $C_{10}H_{15}NO_4$: C, 56.32; H, 7.09; N, 6.57. Found: C, 56.61; H, 7.00; N, 6.71.

1-Acetyl-2-methyl-3-pyrrolidone.—A mixture of ethyl 1-acetyl-5-methyl-4 oxo-3-pyrrolidinecarboxylate (88.3 g., 0.41 mole) and 400 ml. of water containing 4 ml. of concentrated hydrochloric acid was refluxed for 17 hr. The solution was saturated with sodium chloride and extracted several times with chloroform. The product was isolated from the chloroform extract in the usual manner. It boiled at 83–87° (0.15 mm.), $n^{25}D$ 1.4850; yield, 31.0 g. (55.9%).

Anal. Calcd. for $C_7H_{11}NO_2$: N, 9.92. Found: N, 10.06.

1-Acetyl-2-methyl-3-phenyl-3-pyrrolidinol.—An ethereal solution of phenylmagnesium bromide (0.36 mole) in 240 ml. of dry ether was prepared in the usual manner. The Grignard reagent was treated dropwise with a solution of 1-acetyl-2-methyl-3-pyrrolidone (34.9 g., 0.24 mole) in 80 ml. of anhydrous ether. After being refluxed for 1 hr., the mixture was poured into 300 g. of ice containing 15 g. of ammonium chloride. The ethereal solution was separated and dried over anhydrous magnesium sulfate. The residue obtained after removal of the ether was distilled to obtain 11.0 g. of a fraction, b.p. 155–170° (0.4 mm.). The distillate was dissolved in 100 ml. of acetone. The solution was decolorized with activated carbon, and stored at 0°, to separate 6.6 g. (12.5%) of crystalline product, m.p. 143–145°.

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.49; H, 8.05; N, 6.40.

1-Ethyl-2-methyl-3-phenyl-3-pyrrolidinol.—A solution of 1-acetyl-2-methyl-3-phenyl-3-pyrrolidinol (9.2 g., 0.04 mole) in 50 ml. of tetrahydrofuran was added with efficient stirring over a period of 45 min. to a slurry of lithium aluminum hydride (1.5 g., 0.04 mole) in 50 ml. of tetrahydrofuran. After being stirred and refluxed for 4.5 hr., the mixture was cooled in an ice bath, treated carefully with 2.2 ml. of water, and filtered. The solid cake was extracted with 50 ml. of hot ethanol. The filtrate and the extract were combined and concentrated. 1-Ethyl-2-methyl-3-phenyl-3-pyrrolidinol was collected as a light colored oil by distilling the oily residue under reduced pressure, b.p. 85–93° (0.25 mm.), $n^{25}D$ 1.5372; yield, 5.5 g. (65.8%).

Anal. Calcd. for $C_{13}H_{19}NO$: N, 6.82. Found: N, 7.00.

3-Acyloxy-3-aryl-1-ethyl- or -1-methyl-pyrrolidines and their Hydrochlorides.—3-Aryl-1-ethyl- or -1-methyl-3-pyrrolidinol (0.1 mole), acid anhydride (0.2 mole) and 40 g. of pyridine were mixed and refluxed for 7 hr. While the temperature was kept below 10°, the residue obtained after removal of the excess reagents was dissolved in 25 ml. of water, and the resulting solution was treated with 25 ml. of 40% sodium hydroxide. The mixture was extracted several times with ether. The combined ethereal extracts were dried over anhydrous magnesium sulfate,

filtered and concentrated. The residue was distilled under reduced pressure. The above free base was dissolved in anhydrous ethanol and treated with an equivalent amount of anhydrous hydrogen chloride. The hydrochloride salt was obtained on diluting the solution with anhydrous ether to cloudiness and standing at 0°. Nine 3-acyloxy-3-aryl-1-methylpyrrolidines and one 1-ethylpyrrolidine and their hydrochlorides were prepared in this manner. Their physical constants are tabulated in Table II.

Acknowledgment.—We are indebted to Dr. John W. Kissel and his associates for the pharmacological data.

Structure-Activity Relationships in a Series of Anticonvulsant Bicyclic Acylureas

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The synthesis of a series of monocyclic and bicyclic carbonylureas is reported. The monocyclic carbonylureas containing a hydrogen atom in the *alpha*-position are of no interest as anticonvulsants. 2-Norbornene-5-*endo*-carbonylurea, however, afforded good protection against both electroshock- and pentylenetetrazol-induced convulsions. Introduction of a methyl group *alpha* to the carbonylurea chain of the monocyclic and bicyclic derivatives markedly enhanced anticonvulsant activity. Cycloalkenyl and bicycloalkenyl derivatives were more active than their saturated congeners. Anticonvulsant activity was abolished by the introduction of carboxyl, carbomethoxy or carboximide groupings. N^3-Acetylation reduced activity slightly but significantly increased the duration of action.

As part of an investigation of the contribution of bicyclic nuclei to pharmacodynamically active compounds[2] a series of acylureas derived from bridged bicyclic acids was synthesized. The acylurea radical has long been associated in medicinal chemistry with depression of the central nervous system[3] and Spielman and co-workers[4] have reported the anticonvulsant properties of an extensive series of acylureas derived from alkyl, aralkyl, aryl and heterocyclic carboxylic acids.

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