dimethylamino-*trans*-decalin (0.816 g, 4.45 mmoles) at 0° was added MeI (5 ml) and the reaction mixt stirred in the cold for 30 min, then at 25° for 4 hr. Et_2O was added and the resulting ppt collected by filtration. Recrystn (EtOH–EtAc) afforded 1.20 g (86%) of 1: mp 258–259°; nmr (CD_3OD) δ 3.84 (m, 1 H, C-2 CH), 3.18 (s, 9 H, CH_3). *Anal.* ($C_{13}H_{26}IN$) C, H, I, N.

Enzyme Kinetics. The kinetic measurements were performed as described previously.[4] The concn of AChE (Sigma Chemical Co. electrical eel Type III) was 0.094 μ*M* units/ml of salt soln. The concn of ChE (Sigma Chemical Co., from horse serum, Type IV) was 0.41 μ*M* units/ml. One μ*M* unit hydrolyzes 1 μmole of ACh/min at pH 8.0 and 37°. The salt soln was 0.16 *M* and 0.002 *M* in NaCl and $MgCl_2$, respectively, and contained 50 mg of bovine serum albumin per l. Sigma acetylcholine chloride was used in 6 different concns ranging from 3×10^{-4} to 10×10^{-4} *M* for each detn of K_m and V_{max}. Inhibitor concns were 5×10^{-7} and 5.2×10^{-6} *M*. Measurements were performed by titrating for liberated AcOH under a stream of N_2 using an automatic pH Stat assembly at pH 7.2 ± 0.1 and 24.90 ± 0.05°. Titrant was 0.0100 *M* NaOH. Deionized H_2O was used throughout. Raw data, consisting of a chart trace of per cent of full buret *vs.* time was fitted by an iterative least-squares technique directly to the Michaelis–Menten equation.

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Notes

Spirans. 19. Spirans with Functional Groups[1,†]

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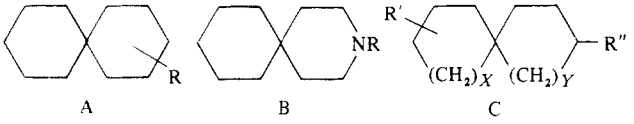
In previous studies,[2,3] it was found that alicyclic spirans A (R = NH_2) substituted in the 2 or 3 position displayed interesting pharmacological properties such as analgetic, analeptic, and local anesthetic actions. In another investigation, a group of N-substituted azaspirans B (R = alkyl, dialkylaminoalkyl, etc.) was synthesized and tested for cytotoxic effects. A number of these compds were found to be highly active.[3,4]



A B C

We would now like to report the preparation and testing of some new substituted spirans of type C where R″ is not an amino group but contains a variety of functional groups such as carboxy and higher homologous acids and their amine derivatives. The general synthetic steps are shown in Schemes I and II in which for simplicity the synthesis of only unsubstituted spirans are given. Many of the spirans prepared have substituents R′ in the first ring of C such as Me, *gem*-Me_2, and CF_3 groups. Besides the preparation of this new class of spiro acids and their intermediates (Table I, 1–18), we were interested in preparing various

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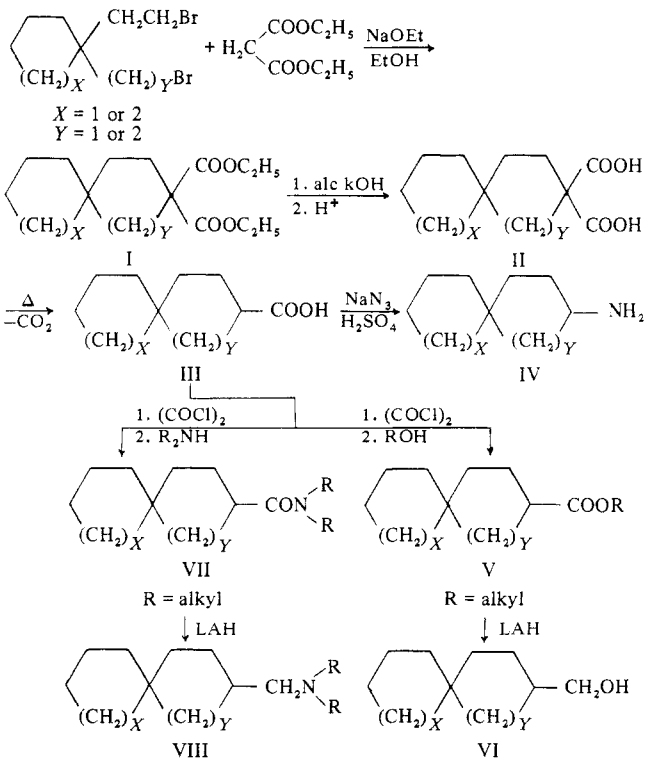
Scheme I

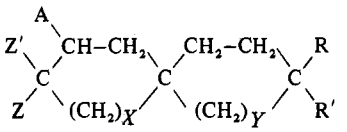


amides and amines of these spiro acids in which the spiran nucleus was separated from the N moiety by 1, 2, or 3 C atoms.

The key compds from which the desired compds could be prepared were spiran carboxylic acid III and spiran acetic acid XII. The acids of type III were synthesized by

alkylation of malonic ester with the appropriate 1,1-bis(bromoalkyl)cycloalkane followed by hydrolysis and decarboxylation. The yields where $Y = 2$ were unusually good due to the *gem*-3,3-dialkyl groupings on the reacting dibromopentane. The reactions of type III acids were normal as expected and are shown in Scheme I in which

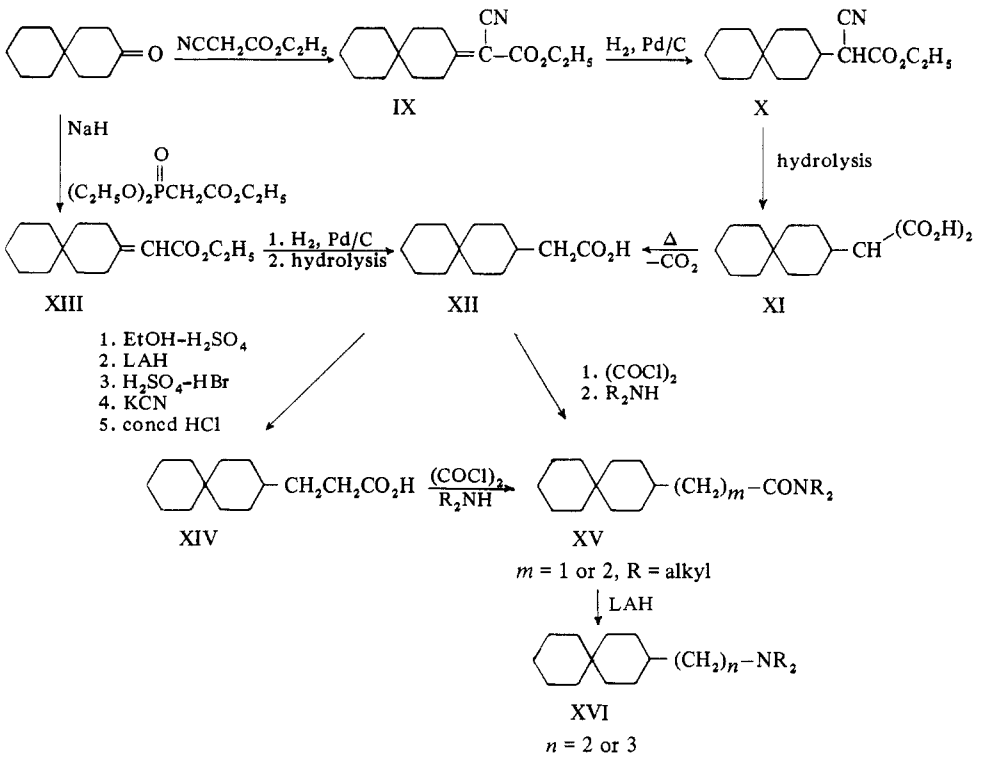
Table I. Substituted Spirans



Compd	A	X	Y	Z′	Z	R	R′	Mp or bp (mm), °C	Empirical formula
1	H	2	2	H	H	$COOC_2H_5$	$COOC_2H_5$	125-127 (0.25)	$C_{17}H_{28}O_4$
2	H	2	2	H	H	COOH	COOH	196-198[a]	$C_{13}H_{20}O_4$
3	H	2	2	H	H	H	COOH	130-135[b] (0.06)	$C_{12}H_{20}O_2$
4	H	1	2	H	H	$COOC_2H_5$	$COOC_2H_5$	120-122 (0.6)	$C_{16}H_{26}O_4$
5	H	1	2	H	H	COOH	COOH	200-201[a]	$C_{12}H_{18}O_4$
6	H	1	2	H	H	H	COOH	128-133[c] (0.6)	$C_{11}H_{18}O_2$
7	H	2	1	H	H	$COOC_2H_5$	$COOC_2H_5$	99-101 (0.1)	$C_{16}H_{26}O_4$
8	H	2	1	H	H	COOH	COOH	173-174[a]	$C_{12}H_{18}O_4$
9	H	2	1	H	H	H	COOH	108-112 (0.1)	$C_{11}H_{18}O_2$
10	H	2	2	CH_3	H	$COOC_2H_5$	$COOC_2H_5$	133-136 (0.6)	$C_{18}H_{30}O_4$
11	H	2	2	CH_3	H	COOH	COOH	200-201[a]	$C_{14}H_{22}O_4$
12	H	2	2	CH_3	H	H	COOH	135-139[d] (0.6)	$C_{13}H_{22}O_2$
13	H	2	2	CH_3	CH_3	$COOC_2H_5$	$COOC_2H_5$	108-113 (0.08)	$C_{19}H_{32}O_4$
14	H	2	2	CH_3	CH_3	COOH	COOH	193-194[a]	$C_{15}H_{24}O_4$
15	H	2	2	CH_3	CH_3	H	COOH	130-135[e] (0.05)	$C_{14}H_{24}O_2$
16	CF_3	2	2	H	H	$COOC_2H_5$	$COOC_2H_5$	130-138 (0.6)	$C_{18}H_{27}F_3O_4$
17	CF_3	2	2	H	H	COOH	COOH	184-185[a]	$C_{14}H_{19}F_3O_4$
18	CF_3	2	2	H	H	H	COOH	114-120[f] (0.08)	$C_{13}H_{19}F_3O_2$
19	H	2	2	H	H	H	COCl	68-70 (0.1)	$C_{12}H_{19}ClO$[y]
20	H	2	2	H	H	H	$COOC_2H_5$	80-85 (0.15)	$C_{14}H_{24}O_2$
21	H	2	2	H	H	H	CH_2OH	87-89 (0.1)	$C_{12}H_{22}O$
22	H	2	2	H	H	H	CH_2COOH	140-142[g] (0.1)	$C_{13}H_{22}O_2$
23	H	2	2	H	H	H	CH_2COCl	81-85 (0.13)	$C_{13}H_{21}ClO$[y]
24	H	2	2	H	H	H	$(CH_2)_2OH$	86-93 (0.05)	$C_{13}H_{24}O$
25	H	2	2	H	H	$=CHCOOC_2H_5$		94-96 (0.03)	$C_{15}H_{24}O_2$
26	H	2	2	H	H	H	$CH_2COOC_2H_5$	92-93 (0.04)	$C_{15}H_{26}O_2$
27	H	2	2	H	H	$=C(CN)COOC_2H_5$		138-142[h] (0.2)	$C_{16}H_{23}NO_2$[z]
28	H	2	2	H	H	H	$CH(CN)COOC_2H_5$	147-149 (0.7)	$C_{16}H_{25}NO_2$[z]
29	H	1	2	H	H	H	COCl	67-68 (0.2)	$C_{11}H_{17}ClO$[y]
30	H	2	2	H	H	H	$(CH_2)_2Br$	74-82 (0.05)	$C_{13}H_{23}Br$
31	H	2	2	H	H	H	$(CH_2)_2CN$	88-93 (0.05)	$C_{14}H_{23}N$[z]
32	H	2	2	H	H	H	$(CH_2)_2COOH$	86.5-87.5	$C_{14}H_{24}O_2$
33	H	2	2	H	H	H	$(CH_2)_2COCl$	140-141 (2.0)	$C_{14}H_{23}ClO$[y]
34	H	2	2	H	H	H	$CONH_2$	159-160	$C_{12}H_{21}NO$[z]
35	H	2	2	H	H	H	CH_2NH_2	248-250[i]	$C_{12}H_{24}ClN$[z]
36	H	2	2	H	H	H	$CON(CH_3)_2$	103-106 (0.04)	$C_{14}H_{25}NO$[z]
37	H	2	2	H	H	H	$CON(C_2H_5)_2$	109-114 (0.05)	$C_{16}H_{29}NO$[z]
38	H	2	2	H	H	H	$CH_2N(CH_3)_2$	53-56 (0.02)	$C_{14}H_{27}N$[j,z]
39	H	2	2	H	H	H	$CH_2N(C_2H_5)_2$	72-78 (0.05)	$C_{16}H_{32}ClN$[k,z]
40	H	1	2	H	H	H	$CON(CH_3)_2$	92-94 (0.03)	$C_{13}H_{23}NO$[l,z]
41	H	1	2	H	H	H	$CH_2N(CH_3)_2$	40-44 (0.02)	$C_{13}H_{25}N$[m,z]
42	H	2	2	H	H	H	$CH_2CON(CH_3)_2$	110-111 (0.02)	$C_{15}H_{27}NO$[n,z]
43	H	2	2	H	H	H	$(CH_2)_2N(CH_3)_2$	62-68 (0.03)	$C_{15}H_{29}N$[o,z]
44	H	2	2	H	H	H	$CH_2CON(C_2H_5)_2$	121-128 (0.05)	$C_{17}H_{31}NO$[z]
45	H	2	2	H	H	H	$(CH_2)_2N(C_2H_5)_2$	87-91 (0.05)	$C_{17}H_{34}ClN$[p,z]
46	H	2	2	H	H	H	$(CH_2)_2N(C_2H_5)_2CH_3$	156-157[a]	$C_{18}H_{36}IN$[q,z]
47	H	2	2	H	H	H	$(CH_2)_2CON(CH_3)_2$	118-123 (0.3)	$C_{16}H_{29}NO$[z]
48	H	2	2	H	H	H	$(CH_2)_2CON(C_2H_5)_2$	128-133 (0.03)	$C_{18}H_{33}NO$[z]
49	H	2	2	H	H	H	$(CH_2)_3N(CH_3)_2$	65-71 (0.03)	$C_{16}H_{31}N$[r,z]
50	H	2	2	H	H	H	$(CH_2)_3N(C_2H_5)_2$	96-99 (0.02)	$C_{18}H_{35}N$[s,z]
51	H	2	2	CH_3	H	H	CH_2OH	96-98 (0.03)	$C_{13}H_{24}O$
52	H	2	2	CH_3	H	H	$COOC_2H_5$	91-94 (0.15)	$C_{15}H_{26}O_2$
53	H	2	2	CH_3	H	H	$CONH_2$	142-143	$C_{13}H_{23}NO$[z]
54	H	2	2	CH_3	H	H	CH_2NH_2	127-130 (2.2)	$C_{13}H_{25}N$[z]
55	H	2	2	CH_3	H	H	$CON(C_2H_5)_2$	124-128 (0.07)	$C_{17}H_{31}NO$[z]
56	H	2	2	CH_3	H	H	$CH_2N(C_2H_5)_2$	114-115 (0.6)	$C_{17}H_{33}N$[t,z]
57	H	2	2	H	H	H	$CO_2(CH_2)_2N(C_2H_5)_2$	170-171	$C_{18}H_{34}ClNO_2$[u,z]
58	H	2	2	H	H	H	$CO_2(CH_2)_2N(CH_3)_2$	175-176	$C_{16}H_{30}ClNO_2$[v,z]
59	H	2	2	H	H	H	$CO_2(CH_2)_2N(C_2H_5)_2$	220-221	$C_{18}H_{34}ClNO_2$[w,z]
60	H	2	2	H	H	H	$CH_2CO_2(CH_2)_2N(C_2H_5)_2$	135-136	$C_{19}H_{36}ClNO_2$[x,z]

[a] mp decomp. [b] mp 77-78°. [c] mp 53-54°. [d] mp 89-90°. [e] mp 133-134°. [f] mp 115-117°. [g] mp 65-66°. [h] mp 54-55°. [i] mp HCl; calcd, Cl, 16.13; found, Cl, 16.09. [j] mp HCl, 285-286°, calcd, $C_{14}H_{28}ClN$; Cl, 14.42; found, Cl, 14.38. [k] mp HCl, 181-182°; calcd, Cl, 12.95; found, 13.08. [l] mp 76-77°. [m] mp HCl, 285-286°; calcd, $C_{13}H_{26}NCl$: Cl, 15.29; found, Cl, 15.08. [n] mp 45-46. [o] mp HCl, 255-256°. [p] mp HCl, 157-158°; calcd, Cl, 12.32; found, 12.28. [q] % iodine. [r] mp HCl, 225-226°. [s] mp HCl, 158°. [t] mp HCl, 171-172°; $C_{17}H_{34}ClN$: calcd, Cl, 12.30; found, 12.14. [u] Calcd, Cl, 10.68; found, Cl, 10.72. [v] Calcd, Cl, 11.66; found, Cl, 11.93. [w] Calcd, Cl, 10.31; found, Cl, 10.33. [x] Calcd, Cl, 10.25; found, 10.14. [y] % chlorine. [z] All compds were analyzed for C, H; those with footnote *z* also for N.

Scheme II



alcohols, esters, amides, and amines were produced. 3-Carboxyspiro[5.5]undecane was converted *via* the Schmidt reaction to the known 3-aminospiro[5.5]undecane previously obtained by another route.[2] The 3-aminospiro[5.5]undecane from both methods was identical as confirmed by bp, spectra, and mmps of its derivatives.

In Scheme II is shown the synthesis of spiran acetic acid XII and spiran propionic acid XIV. The spiro ketone was easily converted into its α-cyanocycloalkylidene derivative IX and hydrogenated to X. Somewhat surprisingly, hydrolysis of X by concd HCl or 40% H_2SO_4 did not yield XI or XII. However, the mixt obtained by hydrolysis when subjected to further hydrolysis by 15–20% alkali gave XI which on pyrolysis smoothly gave the acid XII. A more satisfactory route to XII was achieved by means of the Emmon's modification of the Wittig reaction to produce XIII. Hydrogenation and hydrolysis readily produced the desired acid XII. In order to extend this chain by 1 C, the acid XII was esterified and reduced to the corresponding alcohol by LAH. The alcohol on treatment with a mixt of H_2SO_4 and HBr produced the bromide which with KCN gave the nitrile. This on treatment with concd HCl yielded the β-(spiro[5.5]undecyl)propionic acid XIV. All other reactions shown in Scheme II were normal as expected. The propionic acid XIV was converted *via* the amide to the corresponding spiran propylamine XVI.

The acid chlorides **19**, **23**, **29**, and **33** were not subjected to tests due to their instability. The other 56 compds were tested for cytotoxic action against lymphosarcoma or breast tissue culture cells. None of these compds showed appreciable activity. The same compds when screened for analgetic action[2] and antiinflammatory action employing the granuloma pouch method displayed no significant activity.

Experimental Section

Elemental microanalyses were performed by Schwarzkopf Microanalystical Laboratory, Woodside, N. Y. All melting points (Thomas-Hoover capillary-type apparatus) are corrected. The ir spectra of all compds corresponded with assigned structures. In Table I where analyses are indicated only by symbols of the elements, analytical results obtained for those elements were within ±0.4% of the theoretical values. Representative examples are given for each type of compd. All arabic numbered compds refer to the respective compd in Table I.

3,3-Dicarboethoxyspiro[5.5]undecane (1). To 250 ml of abs EtOH was added 10.12 g (0.44 g-atom of Na. After the Na was dissolved, 35.4 g (0.23 mole) of diethyl malonate was rapidly added and the mixt was stirred at reflux for 15 min. 1,1-Bis(β-bromoethyl)cyclohexane (60 g, 0.2 mole) was added as rapidly as possible and the mixt was refluxed for 24 hr. It was cooled, acidified with 10% HCl, dild with H_2O to dissolve the salt, and extd twice with Et_2O. The Et_2O soln was washed with H_2O and satd NaCl soln, dried ($MgSO_4$), and stripped. Distn (17 mm) after a forerun gave the crude material above 150°. Redistn gave 42 g (71%) of product, bp 123° (0.2 mm).

3,3-Dicarboxyspiro[5.5]undecane (2). The diester **1** (39.0 g, 0.131 mole) was refluxed for 2 hr with a soln of 37.5 g of KOH in 400 ml of abs EtOH. After cooling, the salt was filtered, washed twice with abs EtOH, and dissolved in 400 ml of H_2O. The soln was treated with charcoal, filtered, and acidified with 10% H_2SO_4. The crude acid, after filtering, washing with H_2O, and drying, weighed 25.5 g (80.1%), mp 179–180° dec. A sample was recrystd 3 times from 20% EtOH, mp 197–198° (gas evoln).

3-Carboxyspiro[5.5]undecane (3). The diacid **2** (24.5 g, 0.102 mole) melted and CO_2 was evolved at 185°. After raising the temp to 200° for 1 hr the product was distd, bp 126–132° (0.05 mm), 18.6 g (93%), mp 74.5–77°. Recrstn from EtOAc–C_6H_6 gave mp 77–78°.

3-Aminospiro[5.5]undecane (IV, X = 2, Y = 2). To a stirred mixt of 4.3 g (0.03 mole) of **3** dissolved in 41 ml of concd H_2SO_4 and 80 ml of $CHCl_3$ was added in small portions of 2.3 g of NaN_3 at 45°. The mixt was then heated to reflux for 30 min and then dild with 200 g of ice. With cooling the reaction mixt was neutralized with 15% NaOH and extd 3 times with Et_2O. The exts were extd 3 times with 10% HCl and the acid soln was made basic and extd 3 times with Et_2O. The Et_2O soln was washed with satd NaCl soln, dried, and stripped. The residue distd at 90–92° (4.0 mm) yielding 2.8 g (55.7%). The HCl, picrate, and phenylthiourea derivatives all melted as previously reported,[2] no depression of mmp. The ir spectra of the amine and its salts were identical.

Spiro[5.5]undecyl-3-carbonyl Chloride (19). To a soln of 30.0 g (0.152 mole) of acid **3**, dissolved in 150 ml of C_6H_6, was slowly added 25 g of $(COCl)_2$ and the mixt was refluxed for 1 hr. The solvent and excess $(COCl)_2$ were removed, and the residue was distd, bp 68–70° (0.1 mm), 31.8 g (96.9%).

***N,N*-Diethyl-3-carboxamidospiro[5.5]undecane (37).** The

acid chloride **19** (10.7 g, 0.05 mole) was treated in C_6H_6 with excess of Et_2NH (0.1 mole) and refluxed for 1 hr. The soln was dild with an equal vol of anhyd Et_2O and filtered. The filtrate was washed with 5% HCl, H_2O, and satd salt soln and dried (Na_2SO_4). The solvent was stripped and distd 9.8 g (70.8%), bp 109–114° (0.05 mm).

3-(*N,N*-Diethylaminomethyl)spiro[5.5]undecane (39). The amide **37** (6.9 g, 0.0273 mole) was reduced to the amine in the usual manner in Et_2O with LAH. After the usual work-up the product distd at 72–78° (0.05 mm), 5 g (76.8%), and was converted into its HCl salt, mp 181–182°.

Diethylaminoethyl ester of 3-carboxyspiro[5.5]undecane (57) was prepd by refluxing in C_6H_6 equimolar amts of the acid chloride **19** and diethylaminoethanol. After the usual work-up, the product when recrystd from EtOH–Et_2O had mp 170–171°.

3-Carboethoxyspiro[5.5]undecane (20). A mixt of acid chloride **19** (30 g, 0.139 mole) in 150 ml of C_6H_6 was treated with 50 ml of abs EtOH and refluxed for 0.5 hr. The solvent was removed and the product distd, bp 80–85° (0.15 mm), 26.9 g (86.2%).

3-Hydroxymethylspiro[5.5]undecane (21). The reduction of the ester **20** (25.9 g, 0.115 mole) in Et_2O by LAH gave the product, 20 g (95.8%), bp 87–89° (0.1 mm).

Ethyl 2-Cyano-2-(spiro[5.5]undec-3-yl)acetate (28). A soln of 64.7 g (0.247 mole) of ethyl 2-cyano-2-(spiro[5.5]undecylidene-3-yl)acetate[5] dissolved in 300 ml of abs EtOH was hydrogenated at room temp using 3 g of 10% Pd/C. H_2 uptake was 1.8 kg/cm² (theory 1.7 kg/cm²). After filtering and removal of solvent the residue was distd, bp 147–149° (0.7 mm), to yield 56.8 g (87.3%).

Spiro[5.5]undec-3-ylacetic Acid (22). The cyano ester **28** (56.0 g, 0.21 mole) was refluxed with 300 ml of concd HCl for 24 hr and dild with 300 ml of H_2O. The white gummy material was exted with Et_2O and the Et_2O was evapd. This material was dissilved in a soln of 60 g of KOH in 400 ml of abs EtOH and refluxed for 20 hr. The EtOH was evapd and the K salt was dissolved in H_2O, decolorized by charcoal, and acidified with HCl. The slightly brown ppt of this malonic acid derivative was filtered and dried (mp 143°), 48 g. It was heated at 200° until evoln of CO_2 ceased. The residue was distd, bp 140–142° (0.1 mole), 28 g (55%).

Ethyl (spiro[5.5]undecylidene-3-yl)acetate (25) was prepd from 27 g (0.162 mole) of spiro[5.5]undecan-3-one and triethyl phosphonoacetate as outlined by Wadsworth and Emmons.[6] The product was distd, bp 94–96° (0.03 mm), 27.4 g (71.7%).

Ethyl (Spiro[5.5]undec-3-yl)acetate (26). The unsat ester **25** (47.25 g, 0.2 mole) was hydrogenated in the same manner as **28**. The uptake of H_2 was 1.1 kg/cm² and the product distd, bp 92–93° (0.04 mm), to yield 45.5 g (95.4%). Hydrolysis readily gave **22**.

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Antiinflammatory 2,3-Dihydro-2-oxobenzofuran-3-carboxanilides

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The discovery,[1] made in these laboratories, that certain β-oxoanilides, *e.g.*, dioxoisoquinoline-4-carboxanilides, which display unusually strong acidic properties also manifest potent antiinflammatory activity has been confirmed in more recent publications.[2-4] The purpose of this communication is to extend these findings by describing the synthesis and some chemical and biological properties of a series of novel carboxanilides derived from 2(3*H*)-benzofuranone (I).

Treatment of I with aryl isocyanates under basic conditions led to the desired 2,3-dihydro-2-oxobenzofuran-3-carboxanilides (Table I). Best yields of the carboxanilides were obtained using an inverse addition procedure in which incipient carbanion derived from I was generated in the presence of excess isocyanate. This procedure presumably minimized a competing reaction in which I undergoes base-catalyzed self-condensation to form II.[5] Only the latter material was isolated when I was allowed to react with diethyl carbonate, a relatively poor electrophile.

The 2,3-dihydro-2-oxobenzofuran-3-carboxanilides display acidic properties (pK_a' 3–4) comparable to those seen in an earlier series.[1,6] Inspection of Ealing-Corey-Pauling-Koltun space-filling molecular models indicates that formation of the resonance-stabilized enol tautomer (III) appears to be precluded because of the severe steric interaction which would be generated between the protons attached to the amide nitrogen and position four of the benzofuranone nucleus. This assumption is confirmed by examination of the nmr and ir spectra. The nmr spectra exhibit signals at *ca.* δ 4.7 representing the proton at position 3 while the ir spectra show strong carbonyl absorptions at *ca.* 5.5 and 6.0 μ. They are, therefore, consistent with the presence of the keto tautomer rather than of III. Rehybridization of the lone sp^3 C at position 3 may be accommodated, however, by ionization in which stability of the resulting anion (IV) is very likely favored by the formation of a H bond between the enolate anion and the proton on the amide N. Thus, both steric hindrance to enolization and enhanced enolate anion stability probably contribute to the singularly acidic characteristics of these carboxanilides.

Antiinflammatory activity was measured by the carrageenin-induced rat foot edema assay.[7] All compounds in Table I demonstrated activity at least equivalent to that evinced by aspirin. In addition, compds **2**, **5**, and **13** exhibited activity at 10 mg/kg equivalent to that shown by aspirin at a dose of 100 mg/kg.

Experimental Section

Melting points are uncorrected. Isocyanates used were commercial materials as was 2-hydroxyphenylacetic acid. Nmr spectra were recorded on a Varian A-60 spectrometer (Me_4Si). pK_a' detns were performed at 25° in 1:2 (v/v) H_2O–dioxane using a Metrohm automatic potentiograph (Model E 436). Compds for which no pK_a' data are reported were insufficiently soluble. Where analyses are indicated only by symbols of the elements, results obtd were within ±0.4% of calcd values.

2(3*H*)-Benzofuranone (I). A soln of 38.0 g (0.25 mole) of 2-hydroxyphenylacetic acid in 500 ml of xylene contg a catalytic amt of *p*-TsOH was refluxed for 1.5 hr under a Dean–Stark trap. After evapn of the xylene the residual oil was distd to yield 30.0 g (90%) of I, bp 132–134° (18 mm), mp 43–45° (lit.[8] mp 49°).

5-Chloro-2-hydroxyphenylacetic acid was prepd from 5-chloro-2-methoxybenzaldehyde[9] according to the method of Levine, *et al.*,[10] for the prepn of 2-hydroxyphenylacetic acid, mp 128–129.5°. *Anal.* ($C_8H_7ClO_3$) C, H.

5-Chloro-2(3*H*)-benzofuranone. Prepared as described above for 2(3*H*)-benzofuranone except that PhH was used in place of xylene, mp 127–129°. *Anal.* ($C_8H_5ClO_2$) C, H.

Method A. A soln of lactone in DMF was added to a cold suspension of an equimolar amount of a mineral oil dispersion of NaH in DMF. Gas was liberated; immediately after addn was complete the appropriate isocyanate was added dropwise. Tlc at this point showed no starting material remaining and the reaction mixt was