4,7-Dihydro-3a,7a-indandicarboximide (XIV).—A mixture of 100 g of 2-cyanocyclopentene-1-carboxylate and 250 ml of butadiene was heated at 175° in a bomb for 22 hr. On cooling, the contents of the bomb were poured into 8 l. of acetone. The cloudy solution was filtered and taken to dryness *in vacuo* to leave 150 g of dark oil. This was poured into 2 l. of 95% ethanol and filtered again through Super-Cel. The clear yellow solution was taken to dryness and the resulting oil distilled *in vacuo*.

The first fraction weighing 59 g boiled over a range from below 100 to 115° (0.7 mm). The next fraction weighing 15 g boiled from 115 to 125° (0.6 mm) and contained the desired nitrile ester as indicated by infrared and nmr analysis.

This nitrile ester was cyclized by the procedure of Horning and Schock.[11] The mixture of 5 g of cyano ester, 25 ml of glacial acetic acid, and 25 ml of concentrated HCl was heated on the steam bath for 2 hr. The resulting solution was cooled and poured into 250 ml of water, and the oil which separated was extracted three times with 50-ml portions of $CHCl_3$. The extracts were dried (Na_2SO_4) and evaporated to dryness. The resulting yellow oil weighed 4.8 g and crystallized on standing. Recrystallized from CCl_4, it weighed 0.86 g, mp 152–156°. The infrared spectrum showed typical dicarboximide absorption. The dicarboximide was recrystallized twice more from CCl_4 to a melting point of 162–164°.

4,7-Dihydro-N-methyl-3a,7a-indandicarboximide was prepared by treating 166 mg of dicarboximide with excess ethereal CH_2N_2. It was recrystallized from petroleum ether (30–60°) to yield 116 mg, mp 84–87°. Its infrared spectrum was consistent.

2,3-Epoxy-1,2,3,4,5,6,7,8-octahydro-4a,8a-naphthalenedicarboximide (XII).—To a solution of 10 g of II in 200 ml of CH_2Cl_2, was added 10 g of *m*-chloroperbenzoic acid and the resulting solution was stirred at room temperature overnight. The reaction solution was washed three times with $NaHCO_3$ solution, dried (Na_2SO_4), and taken to dryness. The white crystalline residue was recrystallized from $CHCl_3$ to yield 4.6 g, mp 225–226°. Further crystallizations raised the melting point to 230–231°. The infrared and nmr spectra were consistent with the proposed structure.

2,3-Epoxy-1,2,3,4,5,8-hexahydro-4a,8a-naphthalenedicarboximide (XI) was prepared in the same manner as XII using only 1 mole of *m*-chloroperbenzoic acid/mole of dicarboximide I. The product proved to be a mixture of starting material and monoepoxide. The epoxy compound was finally obtained in pure form (11% yield) by fractional crystallization and silicic acid chromatography. It had mp 228–230°, and its spectra were consistent.

Pharmacology.—Adult male mice weighing 18–24 g were used in all the pharmacological testing. ED_{50} values were calculated by the method of Litchfield and Wilcoxon.[18]

Hexobarbital Sleeping Time (HST).—Groups of four mice were injected intraperitoneally with the test compound 30 min before the intraperitoneal injection of 100 mg/kg of hexobarbital. The time in minutes between the injection of the hexobarbital and the regaining of the righting reflux was measured and compared to that of the control group.

Maximal Electroshock Test (MES).—The compounds to be tested were injected intraperitoneally to groups of four mice, 1 hr prior to being subjected to supramaximal electroshock as per the method of Swinyard, *et al.*[19] The results are expressed as a ratio of the number of animals protected from the hind limb extensor phase of the seizure to the number shocked.

Strychnine Lethality Test (SLT).—Groups of four or ten mice were administered the test compounds 30 min prior to the intraperitoneal injection of 2 mg/kg of strychnine sulfate. The animals were observed for death during the 30 min following strychnine. The results are expressed as a ratio of the number of animals surviving strychnine to the number of animals tested.

Pentylenetetrazole Test (MET).—Thirty minutes following the injection of the test compound, groups of four to ten mice were injected subcutaneously with 85 mg/kg of pentylenetetrazole. The results are expressed as a ratio of the number of animals protected from the clonic convulsions induced by pentylenetetrazole to the number of animals tested.

Acknowledgments.—We wish to thank Mr. J. Davisson for preparing some of these compounds, Mrs. B. Carter for obtaining the animal test results, and Dr. J. C. Little (E. C. Britton Laboratory, The Dow Chemical Company, Midland, Mich.) for the large-scale Diels–Alder preparations. We also appreciate the assistance of Dr. J. P. Heeschen (Chemical Physics Laboratory, The Dow Chemical Co., Midland, Mich.) in the nmr spectral interpretations.

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(19) S. A. Swinyard, W. C. Brown, and L. S. Goodman, *ibid.*, **106**, 319 (1952).

Preparation and Anticonvulsant Activity of Some Aryldialkylsuccinimides

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A series of substituted succinimides related to α-methyl-α-phenyl-β-ethylsuccinimide has been prepared and examined for anticonvulsant properties.

The interesting tranquilizing properties of α-methyl-α-phenyl-β-ethylsuccinimide[2] prompted us to prepare a series of closely related compounds. Many of these showed activity against pentylenetetrazole-induced convulsions and some showed activity against electrically induced convulsions.

Most of the compounds were synthesized by the method of Miller and Long[3] as modified by Miller and Hull[2] in which a ketone is condensed with ethyl cyanoacetate to yield an α-cyanocinnamate. This is then treated with KCN, followed by an alkyl halide, and thus converted to an α,β-dicyanopropionate which was hydrolyzed directly to a succinimide with KOH in aqueous alcohol.

Neither Scheme I nor the sequence[4] arylacetonitrile → alkylarylacetonitrile → ethyl α-aryl-α,β-dialkylsuccinic-α-nitrile β-ester → succinic acid → succinimide was found convenient for the preparation of aryldialkylsuccinimides with larger or functional α substituents. The desired compounds were prepared by condensing the appropriate arylacetonitrile with an aldehyde in the presence of NaCN to give an arylalkylsuccinonitrile[5] which was then alkylated with an alkyl halide using NaH in tetrahydrofuran (THF) (Scheme II). The resulting aryldialkylsuccinonitrile was hy-

(1) To whom inquiries should be addressed at E. R. Squibb and Sons, New Brunswick, N. J.

(2) C. A. Miller and R. L. Hull, U. S. Patent 3,183,245 (1965).

(3) C. A. Miller and L. M. Long, *J. Am. Chem. Soc.*, **75**, 6256 (1953).

(4) R. Robbin, *Bull. Soc. Chim. France*, 2275 (1965).

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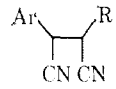
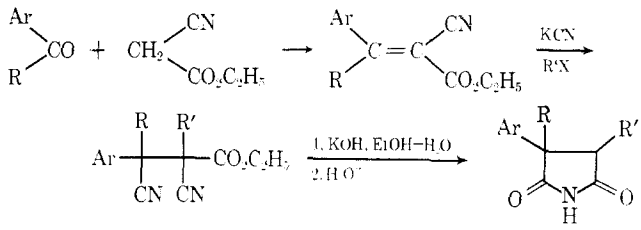
TABLE I
α-ARYL-β-ALKYLSUCCINONITRILES



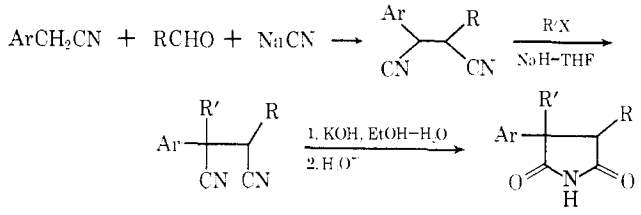
Ar	R	Yield, %	Mp or bp, °C (mm)	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
C_6H_5	H	61	68–69[a]	$C_{10}H_8N_2$						
C_6H_5	CH_3	53	125–128 (0.5)	$C_{11}H_{10}N_2$	77.62	5.92	16.46	77.56	6.03	16.58
C_6H_5	C_2H_5	40	50–52[b]	$C_{12}H_{12}N_2$	78.23	6.56	15.21	78.13	6.64	15.30
p-ClC_6H_4	CH_3	55	141–143[b]	$C_{11}H_9ClN_2$	64.55	4.44	13.69	64.67	4.51	13.56
p-ClC_6H_4	C_2H_5	79	136–138[c]	$C_{12}H_{11}ClN_2$	65.91	5.07	12.81	66.15	5.21	12.67
p-FC_6H_4	CH_3	52	114–116[c]	$C_{11}H_9FN_2$	70.20	4.82	14.88	70.15	4.87	14.91
p-FC_6H_4	C_2H_5	73	115–117[b]	$C_{12}H_{11}FN_2$	71.27	5.48	13.85	71.33	5.61	13.94
C_6H_5	i-C_3H_7	50	138–140[b]	$C_{13}H_{14}N_2$	78.74	7.12		78.59	7.25	
p-$CH_3OC_6H_4$	C_2H_5	39	97–99[b]	$C_{13}H_{14}N_2O$	72.87	6.58	13.07	73.04	6.74	13.14

[a] Reference 11. [b] Recrystallized from benzene–petroleum ether (bp 30–60°). [c] Recrystallized from ethanol.

SCHEME I



SCHEME II



drolyzed to the corresponding succinimide with KOH in aqueous alcohol.[2] This method for preparing arylalkylsuccinonitriles is considerably shorter than previous methods involving t-butylcyanoacetate[6] and gives much better yields than the controlled basic hydrolysis of dicyanopropionates. The latter procedure, however, using KCN as the base is a good method for arylsuccinonitriles without β substituents.[7]

The initial condensation in Scheme II was successful with simple aliphatic aldehydes but not with conjugated or t-aminoaldehydes of the aliphatic series. Acetone also failed to yield dinitrile. In some cases, considerable amounts of olefins were isolable. The alkylation of the intermediate arylsuccinonitrile required a fairly active halide for success; otherwise, olefin formation took place. With chlorides no reaction occurred. Introduction of the alkyl groups in the reverse order using α-aryl-α-alkylsuccinonitriles was unsuccessful under these conditions, and olefin was obtained as the sole product. The direct hydrolysis of the succinonitriles to succinimides using base in aqueous alcohol was often incomplete, particularly when the α-alkyl group was larger than methyl. In these cases, the acidified reaction mixture was heated to effect complete hydrolysis. Recently, alcoholic acid has been used for the direct conversion of succinonitriles to succinimides.[8]

Table I lists the intermediate α-aryl-β-alkylsuccinonitriles prepared in this study together with their physical data. In Table II are collected the physical and biological data for all of the aryldialkylsuccinimides prepared by methods I or II.

Pharmacology.—The succinimides prepared were tested for their anticonvulsant activity by a method[9] described earlier. While none of the compounds was found to be superior to α-methyl-α-phenyl-β-ethylsuccinimide in these tests, a number of structure–activity relationships are discernable. Among the aromatic substituents studied, only m- and p-monohalides showed comparable antipentylenetetrazole activity, while o-halides, which did not show appreciable antipentylenetetrazole activity, did show comparable antielectroshock activity. Both the α-methyl and β-ethyl groups appear to be of optimum size since larger groups in either position caused activity to fall off rapidly. Functionality, even a simple olefinic group, also generally decreased activity.

Experimental Section[10]

General Procedure for Scheme I. α-p-Fluorophenyl-α-methyl-β-ethylsuccinimide. A. Ethyl α-Cyano-p-fluoro-β-methylcinnamide.—A mixture of 100 g (0.725 mole) of p-fluoroacetophenone (Pierce Chemical Co.), 82 g (0.725 mole) of ethyl cyanoacetate, 13 g of β-alanine, and 36 g of glacial acetic acid in 150 ml of benzene was heated under reflux for 24 hr while 19 ml of aqueous phase collected in the H_2O trap. The mixture was cooled and washed three times with H_2O. The aqueous washings were washed with benzene, and the combined organics distilled. After recovered starting materials, there was collected 131 g of product at 128–131° (0.65 mm).

Anal. Calcd for $C_{13}H_{12}FNO_2$: C, 66.94; H, 5.19. Found: C, 67.07; H, 5.07.

B. Ethyl α-Ethyl-β-p-fluorophenyl-β-methyl-α,β-dicyanopropionate.—A solution of 116.5 g (0.50 mole) of the previous compound in 400 ml of absolute ethanol was stirred and treated with 36 g (0.535 mole) of KCN, then stirred under reflux for 0.5 hr. The mixture was then cooled somewhat and treated with 65.5 g (0.60 mole) of CH_3CH_2Br. The resulting mixture was stirred under reflux overnight then filtered hot. The filtrate was taken to dryness, triturated several times with petroleum ether (bp 30–60°), then crystallized from ethanol–H_2O to yield

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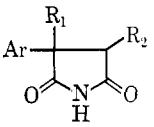
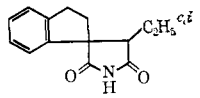
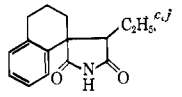
(9) G. Chen and C. R. Ensor, *A.M.A. Arch. Neurol. Psychiat.*, **63**, 56 (1950).

(10) Melting points were taken in open glass capillaries using a Thomas–Hoover Unimelt apparatus and are uncorrected.

TABLE II
ARYLDIALKYLSUCCINIMIDES



Ar	R_1	R_2	Mp or bp, °C (mm)	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H	Anticonvulsant act. pentylenetetrazole[a]	PD_{50}, mg/kg[b]
C_6H_5[c]	CH_3	C_2H_5	65–66.5	$C_{13}H_{15}NO_2$[d]					4+/32	50–100
p-$NH_2C_6H_4$[c]	CH_3	C_2H_5	142–144	$C_{13}H_{16}N_2O_2$	67.22	6.94	67.43	6.85	0/500	200–400
p-$C_6H_5CH_2OC_6H_4$[c]	CH_3	C_2H_5	123–129	$C_{20}H_{21}NO_3$	74.28	6.54	74.14	6.52	0/500	>400
p-BrC_6H_4[c]	CH_3	C_2H_5	61–62	$C_{13}H_{14}BrNO_2$	52.72	4.77	52.70	4.72	4+/63 3+/32	100–200
o-ClC_6H_4[c]	CH_3	C_2H_5	210–212	$C_{13}H_{14}ClNO_2$	62.03	5.61	62.00	5.25	0/500	50–100
m-ClC_6H_4[c]	CH_3	C_2H_5	189–192 (0.7)	$C_{13}H_{14}ClNO_2$	62.03	5.61	62.23	5.80	4+/125	100–200
p-ClC_6H_4[c]	CH_3	C_2H_5	182–185 (0.1)	$C_{13}H_{14}ClNO_2$	62.03	5.61	62.27	5.85	4+/63	100–200
p-ClC_6H_4[e]	CH_3	CH_3	146–149	$C_{12}H_{12}ClNO_2$	60.63	5.09	60.74	5.24	4+/250 3+/125	100–200
2,4-$Cl_2C_6H_3$[c]	CH_3	C_2H_5	168–171	$C_{13}H_{13}Cl_2NO_2$	54.56	4.58	54.58	4.62	2+/250	100–200
3,4-$Cl_2C_6H_3$	CH_3	C_2H_5	144–145	$C_{13}H_{13}Cl_2NO_2$	54.56	4.58	54.57	4.88	0/500	>400
o-FC_6H_4[c]	CH_3	C_2H_5	165–167	$C_{13}H_{14}FNO_2$	66.37	6.00	66.18	6.33	4+/500 3+/250	50–100
m-FC_6H_4[c]	CH_3	C_2H_5	164–169 (0.4)	$C_{13}H_{14}FNO_2$	66.37	6.00	66.17	6.20	4+/63	100–200
p-FC_6H_4[c]	CH_3	C_2H_5	178–180 (0.9)	$C_{13}H_{14}FNO_2$	66.37	6.00	66.32	6.27	4+/32	50–100
p-HOC_6H_4[c,f]	CH_3	C_2H_5	167–177	$C_{13}H_{15}NO_3$	66.93	6.48	67.01	6.78	0/500	>400
o-$CH_3OC_6H_4$[c]	CH_3	C_2H_5	172–173	$C_{14}H_{17}NO_3$	68.00	6.93	68.05	7.16	2+/250	200–400
m-$CH_3OC_6H_4$[c]	CH_3	C_2H_5	190–192 (0.7)	$C_{14}H_{17}NO_3$	68.00	6.93	67.87	6.96	4+/125	~400
p-$CH_3OC_6H_4$[c]	CH_3	C_2H_5	182–184 (0.08)	$C_{14}H_{17}NO_3$	68.00	6.93	67.86	7.03	4+/500	>400
o-$CH_3C_6H_4$[c]	CH_3	C_2H_5	181–182	$C_{14}H_{17}NO_2$	72.70	7.41	72.98	7.73	3+/500	~100
p-$CH_3C_6H_4$[c]	CH_3	C_2H_5	172–178 (0.5)	$C_{14}H_{17}NO_2$	72.70	7.41	72.60	7.60	1+/500	>400
p-$NO_2C_6H_4$[c]	CH_3	C_2H_5	140–145	$C_{13}H_{14}N_2O_4$	59.53	5.39	59.62	5.46	0/500	200–400
m-$CF_3C_6H_4$[c]	CH_3	C_2H_5	180–184 (1.3)	$C_{14}H_{14}F_3NO_2$	58.95	4.94	58.99	5.33	3+/250	100–200
2-C_4H_3O[c,g]	CH_3	C_2H_5	142–145 (0.3)	$C_{11}H_{13}NO_3$	63.75	6.32	64.00	6.55	4+/250 3+/125	200–400
2-C_4H_3S[c,h]	CH_3	C_2H_5	98–100	$C_{11}H_{13}NO_2S$	59.17	5.87	59.39	6.09	4+/250 3+/125	100–200
			170–175 (0.1)	$C_{14}H_{15}NO_2$	73.33	6.59	73.13	6.61	4+/125	100–200
			104–106	$C_{15}H_{17}NO_2$	74.05	7.04	73.96	7.19	0/500	>400
p-ClC_6H_4[c]	C_2H_5	C_2H_5	166–169 (0.3)	$C_{14}H_{16}ClNO_2$	63.27	6.07	63.69	6.35	4+/63	Lethal/200
p-FC_6H_4[c]	C_2H_5	C_2H_5	154–158 (0.3)	$C_{14}H_{16}FNO_2$	67.45	6.47	67.67	6.76	4+/63	100–200
C_6H_5[c]	CH_3	$CH_2CH=CH_2$	165–170 (0.1)	$C_{14}H_{15}NO_2$	73.33	6.59	73.68	6.69	4+/250	100–200
C_6H_5[c]	CH_3	$CH_2C_6H_5$	157–173	$C_{18}H_{17}NO_2$	77.39	6.14	77.14	6.21	2+/500	~400
C_6H_5[c]	CH_3	$CH_2CH=CHCH_3$	158–163 (0.4)	$C_{15}H_{17}NO_2$	74.05	7.04	74.17	7.15	2+/500	~400
C_6H_5[c]	CH_3	$CH_2CCl=CH_2$	127–128	$C_{14}H_{14}ClNO_2$	63.76	5.36	64.03	5.47	0/500	~400
C_6H_5[c]	CH_3	$CH_2CH_2N(C_2H_5)_2$	185–188 (0.1)	$C_{17}H_{24}N_2O_2$	70.80	8.39	71.02	8.67	0/500	>400
C_6H_5[c]	CH_3	$CH_2CHCH_3N(CH_3)_2$	170–172 (0.5)	$C_{16}H_{22}N_2O_2$	70.04	8.08	70.08	8.03	0/500	>400
C_6H_5[c]	CH_3	$CH_2CH_2OCH_2CH_3$	175–180 (0.05)	$C_{15}H_{19}NO_3$	68.94	7.33	69.25	7.41	2+/500	>400
C_6H_5[c]	CH_3	$CH_2CH_2OC_6H_4$-o-OC_2H_5	139–141	$C_{21}H_{23}NO_4$	71.37	6.56	71.70	6.72	0/500	>400
C_6H_5[c]	CH_3	$CH_2C(CH_3)=CH_2$	96–102	$C_{15}H_{17}NO_2$	74.05	7.04	73.82	7.13	0/500	~400
C_6H_5[c]	CH_3	$CH_2CH=C(CH_3)_2$	176–180 (0.3)	$C_{16}H_{19}NO_2$	74.68	7.44	74.56	7.41	2+/500	>400
C_6H_5[c]	CH_3	$CH_2CH=CHCH_2CH_2OCH_3$	196–200 (0.4)	$C_{17}H_{21}NO_3$	71.05	7.37	71.22	7.46	0/500	~400
C_6H_5[c]	CH_3	$CH_2CH_2OC_6H_5$	228–230 (0.1)	$C_{19}H_{19}NO_3$	73.77	6.19	74.07	6.44	2+/500	~400
C_6H_5[c]	CH_3	$CH_2CH=CHC_6H_5$	99–103	$C_{20}H_{19}NO_2$	78.66	6.27	78.39	6.36	0/500	>400
C_6H_5[c]	CH_3	$CH_2CH_2CH_3$	160–165 (0.1)	$C_{14}H_{17}NO_2$	72.69	7.41	72.80	7.63	4+/125	100–200
C_6H_5[e]	CH_3	i-C_3H_7	165–170	$C_{14}H_{17}NO_2$	72.69	7.41	72.41	7.49	4+/125	200–400
C_6H_5[e]	CH_2OCH_3	C_2H_5	125–135[k]	$C_{14}H_{17}NO_3$	68.00	6.93	68.26	7.00	4+/250 3+/125	100–200
p-ClC_6H_4[e]	$CH_2CH=CH_2$	CH_3	132–133	$C_{14}H_{14}ClNO_2$	63.76	5.35	63.50	5.45	4+/500	~200
p-ClC_6H_4[e]	n-C_3H_7[l]	CH_3	142–143	$C_{14}H_{16}ClNO_2$	63.27	6.07	63.38	6.14	2+/500	>400
p-ClC_6H_4[e]	$CH_2CH=CH_2$	C_2H_5	86–98[k]	$C_{15}H_{16}ClNO_2$	64.86	5.80	64.84	5.82	4+/250 3+/125	>400
p-ClC_6H_4[e]	CH_2OCH_3	C_2H_5	182–185 (0.3)[k]	$C_{14}H_{16}ClNO_3$	59.68	5.72	59.88	5.64	4+/500 3+/250	200–400
p-FC_6H_4[e]	$CH_2CH=CH_2$	CH_3	163–164	$C_{14}H_{14}FNO_2$	68.01	5.70	68.07	5.92	0/400	>400
p-FC_6H_4[e]	n-C_3H_7[l]	CH_3	132–134	$C_{14}H_{16}FNO_2$	67.45	6.47	67.42	6.49	1+/500	~400
p-FC_6H_4[e]	$CH_2CH=CH_2$	C_2H_5	174–177	$C_{15}H_{16}FNO_2$	68.93	6.17	68.74	6.23	0/500	>400
p-FC_6H_4[e]	n-C_3H_7[l]	C_2H_5	119–121	$C_{15}H_{18}FNO_2$	68.42	6.89	68.49	7.06	0/500	~400

[a] 4+/32 indicates that a group of five rats is completely protected against a convulsant dose of pentylenetetrazole by 32 mg/kg. [b] PD_{50} indicates the dose necessary to protect 50% of the animals (mice) against electrically induced convulsions. [c] Prepared by Scheme I. [d] Reference 2. [e] Prepared by Scheme II. [f] Prepared by catalytic debenzylation with Pd–C of the O-benzyl compound. [g] $C_4H_3O \equiv$ 2-furanyl. [h] $C_4H_3S \equiv$ 2-thienyl. [i] 4′-Ethylspiro[indan-1,3′-pyrrolidine]-2′,5′-dione. [j] 4′-Ethyl-3,4-dihydrospiro[naphthalene-1(2H),-3′-pyrrolidine]-2′,5′-dione. [k] Purified *via* chromatography on neutral alumina. [l] Prepared by catalytic reduction of the corresponding allyl compound with Raney nickel in 95% EtOH.

94 g of product. A sample recrystallized from benzene–petroleum ether had mp 64–66°.

Anal. Calcd for $C_{16}H_{17}FN_2O_2$: C, 66.65; H, 5.94; N, 9.72. Found: C, 66.92; H, 5.95; N, 9.61.

In many cases this intermediate could not be crystallized and therefore was used crude (ir and nmr spectra indicated at least reasonable purity, however).

C. **α-*p*-Fluorophenyl-α-methyl-β-ethylsuccinimide.**—To a stirred solution of 68 g of KOH in 314 ml of 95% ethanol plus 18 ml of H_2O preheated to 50° was added gradually 72 g (0.25 mole) of the previous intermediate. The resulting solution was stirred under reflux for 6 hr. A precipitate soon began to appear. The hot mixture was filtered and the cake was washed twice with 50 ml of hot 95% ethanol. The combined filtrates were concentrated to *ca.* 150 ml at the water pump below 40°. An equal volume of H_2O was added, and the solution was treated dropwise with 60 ml of 37% HCl below 30–35°. The product was extracted with three portions of ethyl acetate, and these were combined and washed repeatedly (saturated Na_2SO_4). The extracts were then dried and evaporated. The residue was taken up in 500 ml of ether, the small insoluble precipitate was filtered off, and the residue on evaporation distilled; 28 g of product was collected at 170–180° (1.2 mm); redistilled, it had bp 178–180° (0.9 mm).

α-*p*-Aminophenyl-α-methyl-β-ethylsuccinimide.—A solution of 26.2 g (0.1 mole) of α-methyl-α-*p*-nitrophenyl-β-ethylsuccinimide in methanol was shaken with 20% Pd–C under 3 atm of hydrogen until uptake was complete. Filtration and evaporation of the filtrate left a crystalline residue in quantitative yield. Recrystallized from ethanol it had mp 142–144°.

α-Methyl-α-*p*-nitrophenyl-β-ethylsuccinimide.—To 200 ml of fuming (90%) nitric acid stirred and cooled to −30 to −40° was added portionwise 65 g (0.30 mole) of α-methyl-α-phenyl-β-ethylsuccinimide. Each addition produced an orange coloration which soon faded. After the addition was completed, the mixture was allowed to warm up to −25° and poured onto ice. Filtration left 133 g of crude damp product. A sample recrystallized twice from ethanol–water had mp 140–145°.

Phenylsuccinonitrile.—A mixture of 318 g (3.0 moles) of benzaldehyde, 339 g (3.0 moles) of ethyl cyanoacetate, 500 ml of absolute ethanol and 6 ml of piperidine was stirred until the temperature returned to 30°. Then 490 g of KCN was added, causing the temperature to rise to 78°. The mixture was treated with 250 ml of water and heated under reflux for 4 hr then cooled and filtered. The filtrates were concentrated at the water pump and diluted with water. The product was extracted with three portions of benzene. The combined extracts were then washed twice with water, once with dilute acetic acid, and again with water. Distillation afforded 290 g of product flash distilled at 160–165° (0.5 mm). Poured into petroleum ether, it soon crystallized; a 286-g yield of product was obtained, mp 68–69°, lit.[11] mp 68–69°.

(11) D. Mowry, *J. Am. Chem. Soc.*, **68**, 2108 (1946).

General Procedure for Scheme II. A. α-Aryl-β-alkylsuccinonitriles.—A mixture of 500 ml of H_2O, 490 g (10 moles) of NaCN, 2500 ml of methanol, and 1.25 moles of the appropriate arylacetonitrile was stirred at 35–40° while a cold solution containing 2.0 moles of the same arylacetonitrile, 3.0 moles of the required aldehyde, and 1 l. of methanol was added dropwise during 2–3 hr at 34–40°. The mixture was then stirred at 35–40° for 2 hr longer, concentrated at the water pump to *ca.* 2 l., and diluted to 5 l. with water added gradually with stirring. The product was then isolated by filtration when crystalline or, if noncrystalline, by extraction with benzene, washing with water and dilute acetic acid, and distillation. Table I lists the α-aryl-β-alkylsuccinonitriles obtained by this procedure together with the crude yields obtained.

B. Aryldialkylsuccinonitriles.—A solution containing 0.25 mole of the appropriate α-aryl-β-alkylsuccinonitriles and excess (usually 0.5 mole) of the desired alkyl halide in 400 ml of THF was stirred and treated portionwise with a 10% excess of 50% NaH (in mineral oil suspension). After the addition was completed, the mixture was stirred under reflux overnight, then cooled and treated cautiously with a few milliliters of H_2O, followed by 25 ml of glacial acetic acid. After removal of solids, the filtrate was taken to dryness at the water pump and the residue was taken up in benzene. After a water washing, the benzene solution was taken to dryness and the crude product was triturated several times with petroleum ether to remove mineral oil. Ir and nmr spectra of the crude products indicated reasonable to excellent purity in each case.

C. Aryldialkylsuccinimides.—To the still warm solution of 30 g of KOH in 300 ml of ethanol plus 30 ml of H_2O was added 0.2 mole of the crude aryldialkylsuccinonitrile gradually with stirring. The mixture was brought to reflux and held there for 6 hr. It was then concentrated at the water pump to one-half volume, diluted with an equal volume of H_2O, acidified with concentrated HCl, and extracted three times with benzene. These extracts were washed with H_2O and taken to dryness. The residue was distilled on the oil pump and the product was crystallized from benzene–petroleum ether or aqueous alcohol. In many cases, the benzene extracts did not contain appreciable desired product due to incomplete hydrolysis under basic conditions. In such cases, the acidified aqueous layer was heated on the steam bath for several hours or longer, then cooled. The product then crystallized out on standing. This was then recrystallized from an appropriate solvent.

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