Acylanthranils. 11. Reaction of Acylanthranils with Alcohols To Give the Corresponding Esters[1]

L. A. Errede,* P. E. Ashley,[2] J. J. McBrady, and D. R. Yarian

3M Central Research Laboratories, St. Paul, Minnesota 55144

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Although the reactions of acetylanthranil (1, R = CH_3) with nucleophilic molecules of the type HNu usually occur "abnormally" via nucleophilic attack at the less electropositive center, C-2 (pathway A, Scheme II), it was shown that reactions of 1 with the anion form, Nu^-, always occur "normally" via nucleophilic attack at the more electropositive center, C-4 (pathway B, Scheme II). Thus, reaction of 1 with ROH in the presence of a small amount of RO^- gives the corresponding *o*-acetamidobenzoate ester 4 in very good yields, rather than the corresponding acetimidate 3. These results are consistent with the hypothesis that the "abnormal" selectivity is attributable to formation of a molecular complex, $1\cdot(HNu)_n$, via hydrogen bonding with the heterocyclic nitrogen atom of 1, which favors subsequent nucleophilic attack at the adjacent electropositive center at C-2. Since Nu^- cannot be restrained by the tether of hydrogen bonding to the electron donating atoms of 1, reaction occurs "normally" via direct nucleophilic attack at C-4.

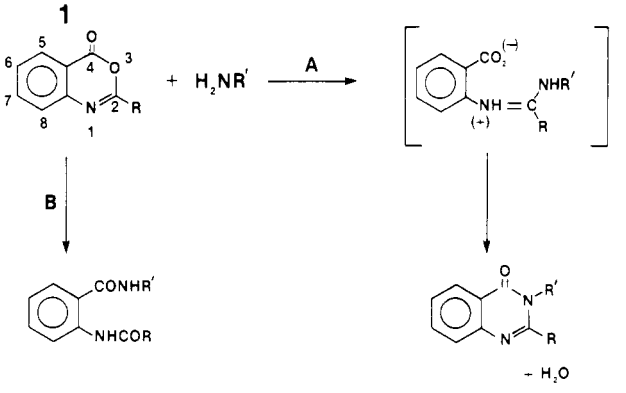
We reported[3] that acetylanthranil (**1a**: 1, R = CH_3) reacts with primary amines via alternate pathways, A and B, to give different products as shown in Scheme I. The formation of the corresponding acetamidine via pathway A is initiated by nucleophilic attack at C-2, whereas formation of the *o*-acetamidobenzamide via pathway B is initiated by attack at C-4. Although C-4 is more electropositive than C-2, reaction via pathway A is much more facile than via pathway B unless steric hindrance on the part of the amine impedes nucleophilic attack at C-2. In such cases, reaction follows pathway B, albeit much more slowly than is normal for reaction with small amines.

We suggested[4,5] that the above anomalous results might be due to hydrogen bonding of the coreactant, HNu, with the nucleophilic atoms that bracket the two electrophilic centers of 1 to form a molecular complex $1\cdot(HNu)_n$. Subsequent product formation would occur via intracomplex nucleophilic attack at the nearest electropositive carbon atom. Since the heterocyclic nitrogen is much more nucleophilic than either oxygen atom, hydrogen bonding of HNu with the former predominates, which favors pathway A as outlined in Scheme II. Reaction via pathway B becomes competitive when subsequent nucleophilic attack at C-2 is impeded as stated above.

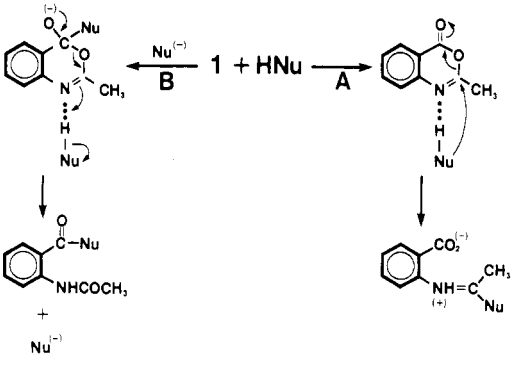
If hydrogen bonding to form **1a**·HNu is indeed responsible for the observed anomalous results, then reaction of **1a** with Nu^- should follow pathway B even when Nu is small. That this may be true is supported by the results observed by Williams and Salvadori,[6] who studied the hydrolysis of **1a** in oxygen-18 enriched water. In acid solution, the product is *o*-$(CH_3CO^*NH)C_6H_4CO_2H$, but in basic solution the product is *o*-$(CH_3CONH)C_6H_4CO^*_2H$, showing that hydrolysis at pH <7 involves nucleophilic attack by HOH at C-2 (i.e., the equivalent of pathway A) whereas hydrolysis at pH >7 involves nucleophilic attack by ^-OH at C-4 (i.e., the equivalent of pathway B).

If one extends this chemistry to include alcohols **2**, then reaction with **1a** should give in neutral (or acidic) solution the corresponding *N*-(2-carboxyphenyl)imidate, **3**, via pathway A and in basic solution the corresponding *o*-acylamidobenzoate ester, **4**, via pathway B.

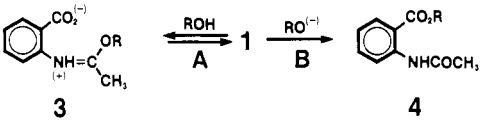
Scheme I



Scheme II



Scheme III



This paper reports the results of our experiments designed to test whether or not the addition of a small amount of ^-OR does indeed alter the pathway selectivity in favor of B and, if successful, how applicable it would be as a general method for synthesis of *o*-(acylamido)benzoate esters.

Results and Discussion

Our initial attempts to effect reaction of acetylanthranil (**1a**) with alcohols such as methanol (**2a**) and ethanol (**2b**)

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(2) Deceased Aug 1, 1974; 3M employee from 1957 to 1967.
(3) Part 4: Errede, L. A.; McBrady, J. J.; Oien, H. T. *J. Org. Chem.* **1977**, *42*, 656.
(4) Part 9: Errede, L. A.; Martinucci, P. D.; McBrady, J. J. *J. Org. Chem.* **1980**, *45*, 3009.
(5) Part 10: Errede, L. A.; McBrady, J. J.; Tiers, G. V. D. *J. Org. Chem.* **1980**, *45*, 3868.
(6) Williams, A.; Salvadori, G. *J. Chem. Soc. B* **1971**, *1105*.

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Table I. Reactions of Acylanthranil, 1, with Alcohol, 2, To Give the Corresponding Esters, 4

	reactants			rxn		product information			
expt	1	2	added base	temp,[a] °C	time, h	4	mp, °C	% yield	key IR absorption data, μm
1	a, acetyl-anthranil	a, CH_3OH	$NaOCH_3$	RT	<0.3	a,a	97-98	91	3.0, 5.9, 6.3, 6.6, 7.8, 7.9, 8.2
2	a, acetyl-antranil	a, CH_3OH	Dabco	RT	1	a,a	97-98	100	3.0, 5.9, 6.3, 6.6, 7.8, 7.9, 8.2
3	a, acetyl-anthranil	b, EtOH	$NaOCH_3$	RT	1	a,b		88	3.1, 5.8, 6.2, 6.5, 7.6-8.2
4	a, acetyl-anthranil	b, EtOH	NaOH	RT	1	a,b	65-66	85	3.1, 5.8, 6.2, 6.5, 7.6-8.2
5	a, acetyl-anthranil	c, *i*-PrOH	NaOPr-*i*	RT	16	a,c	62-63	80	3.0, 5.8, 6.2, 6.5, 7.6, 7.8, 8.1
6	aacetyl-anthranil	d, *t*-BuOH	NaOBu-*t*	reflux	3	a,d	71-72	99	3.1, 5.8, 5.9, 6.3, 6.5, 7.6-8.1
7	a, acetyl-anthranil	e, CH_2=$CHCH_2OH$	NaOR	RT	1	a,e	49.0	80	3.1, 5.8, 5.9, 6.2, 6.5, 7.7, 7.9, 8.0
8	a, acetyl-anthranil	f, PhOH	NaOPh	reflux	3	a,f	95-96	96	3.0, 5.8, 5.9, 6.2, 6.5, 7.7, 7.8, 8.0
9	a, acetyl-anthranil	g, $HO(CH_2)_6OH$	pyridine	RT	<0.5	aa,g	136-138	94	3.1, 5.8, 5.9, 6.2, 6.5, 7.7, 7.8, ,.0
10	a, acetyl-anthranil	h, $(p\text{-}HOPh)_2C(CH_3)_2$	pyridine	reflux	3	aa,h	222-228	95	3.0, 5.8, 5.9, 6.2, 6.5, 7.6-8.3
11	a, acetyl-anthranil	k, $Et_2NCH_2CH_2OH$	none	100	1	a,k	oil	100	3.0, 5.8, 5.9, 6.2, 6.5, 7.7-8.1
						a,k·HCl	146-147	85	2.9-4.3, 5.8, 5.9 6.2, 6.5, 7.7-8.0
12	b, (trifluoro-acetyl)anthranil	b, EtOH	NaOEt	RT	<0.5	b,b	80-81	94	3.2, 5.8, 5.9, 6.2, 6.5, 7.9, 8.4, 8.0
13	c, benzoyl-anthranil	g, $HO(CH_2)_6OH$	pyridine	reflux	0.5	cc,g	143-144	76	3.0, 5.9, 6.0, 6.2, 6.5, 7.6-8.1
14	d, methylenebis-(acetylanthranil)	g, $HO(CH_2)_6OH$	pyridine	70	16	cyclic d,g	262-264	93	3.0, 5,8, 5.9, 6.2, 6.5, 7.6-8.0

[a] RT = room temperature.

via pathway A were unsuccessful (i.e., about 90% of **1a** was recovered unchanged even after 8 h in dilute alcohol solution at room temperature). In fact, methyl and ethyl alcohols proved to be good solvents for recrystallization of impure samples of **1a** that contained as much as 25% *o*-acetamidobenzoic acid. Kinetic studies (described in our companion paper, part 12)[7] showed, however, that the acetimidate **3** is indeed formed as expected, but it establishes an equilibrium with **1** and **2** within minutes. Thus the alternate possibilities for reaction with ROH should be written as indicated in Scheme III.

In contrast to the reluctance of **1a** to undergo stable product formation via pathway A in neutral (or slightly acid) alcohol solutions, esterification via pathway B was observed to go rapidly to completion immediately after addition of base. The kinetics of this reaction were monitored by proton NMR and observed to be pseudo first order. The rate of reaction, however, is markedly dependent upon the nature of the added base. For example, the half-life of **1a** in 0.4 M methanol solution is about 8 min in the presence of an equivalent amount of a weak base such as pyridine or 1,4-diazabicyclo[2.2.2]octane (i.e., Dabco), whereas it is less than 15 sec in the presence of an equivalent amount of strong base such as NaOH or $NaOCH_3$. In either case, methyl *o*-acetamidobenzoate is isolated from the methanol solution in very good yield (expts 1 and 2, Table I).

Similar results were noted with ethanol (**2b**), allyl alcohol (**2e**), and β-(diethylamino)ethanol (**2k**) (expts 3, 7, and 11, respectively; Table I). Reaction with **2k** required no additional base, since the presence of the diethylamino group in the β-position of this alcohol was sufficient to ensure nucleophilic attack by ^-OR at C-4 to give β-(diethylamino)ethyl *o*-acetamidobenzoate (**4a,k**) in very good yield.

It was reported[8] that interaction of **1a** with ethanolamine (**2h**) neat gives *o*-acetamido-*N*-(β-hydroxyethyl)benzamide rather than β-aminoethyl *o*-acetamidobenzoate (**4a,h**), showing that reaction with a primary amine occurs preferentially to esterification unless attack by the nucleophilic amine is impeded by steric hindrance. Similarly, a solution of **1a** and an equivalent amount of methylamine in methanol favors interaction with the amine solute over esterification. On the other hand, a solution of **1a** and an equivalent amount of *tert*-butylamine in methanol gives the ester exclusively.

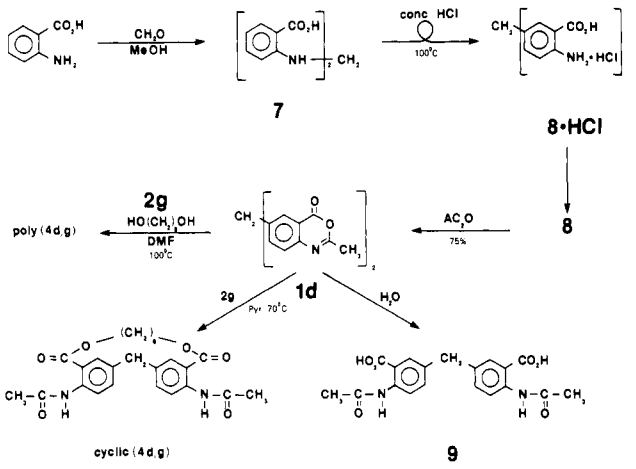
Although nucleophilic attack at C-4 by ^-OR is very facile when R is small, the rate of reaction is slowed considerably when R is large, presumably owing to steric hindrance. Consequently, more strenuous conditions are required with the more bulky alcohols to achieve significant interaction within a reasonable time. Thus, little or no interaction with *tert*-butyl alcohol (**2d**) occurred at room temperature within a 24-h period, whereas the reaction went to completion at reflux within 3 h (expt 6, Table I). Reaction with 2-propanol (**2c**) was intermediate between the two extremes represented by **2a** and **2d**. A good yield of isopropyl *o*-acetamidobenzoate (**4a,c**) was obtained at room temperature (expt 5, Table I), but 16 h were required instead of just minutes as noted with methanol (expt 1). Reflux conditions also appear to be necessary to effect interaction with phenols within a reasonable time interval as noted in expt 8.

Esterification of bifunctional alcohols occurs just as readily as esterification of the corresponding monofunctional alcohol as indicated by the isolation in good yields

(7) Part 12: Errede, L. A.; Hill, J. R.; McBrady, J. J. *J. Org. Chem.*, following paper in this issue.

(8) Part 5: Errede, L. A.; McBrady, J. J. *J. Org. Chem.* **1977**, *42*, 3863.

Scheme IV



of the corresponding diesters of hexamethylene glycol (**2g**) and of 2,2-bis(4-hydroxyphenyl)propane, (**2h**; i.e., Bisphenol-A), which were made to react with 2 equiv of the acylanthranil as noted in expts 9, 10, 13, and 4.

Even poly(vinyl alcohol) (**2i**) and cellulose (**2j**) can be esterified in this way.[9] Esterification occurs randomly to give a modified polymer with pendent *o*-(acylamido)-benzoate groups. The ratio of esterified OH (x) to nonesterified OH ($1 - x$) in the product (i.e., $x/(1 - x)$) increases linearly with the molar charge ratio of reactant 1 to available alcohol groups.

Although the selectivity for interaction of acylanthranils with a given amine is influenced markedly by the substituent at C-2,[10] this is not true in reactions with alkoxides. The reactivity, however, is affected by this substituent as it is in reactions with amines. Reaction of 1 with an alkoxide is always initiated by nucleophilic attack at C-4 to give the corresponding ester regardless of the bulk or the electronic nature of the substituent at C-2. Thus, reactions of ^-OR with (trifluoroacetyl)anthranil (**1b**, 1 with R = CF_3), one of the most reactive acylanthranils, and with benzoylanthranil (**1c**, R = Ph), one of the least reactive acylanthranils, both give the corresponding esters in good yields as noted in Table I, despite the fact that the former reacts with amines via pathway A and the latter via pathway B.[10]

The high yields obtained in this apparently general method for esterification caused us to suspect that it might be used to produce high molecular weight polyesters by reaction of a bis acylanthranil with a bis alcohol or a bis phenol. If successful it would avoid the undesirable weight loss associated with polycondensation of bis acids or bis esters with bis alcohols owing to elimination of volatile products such as H_2O or CH_3OH, respectively. Accordingly, methylenebis(acetylanthranil) (**1d**) was prepared as outlined in Scheme IV. This bifunctional acylanthranil was made to react with an equivalent amount of hexamethylene glycol (**2g**) in dimethylformamide at 100 °C to give the expected polyester (poly-**4d,g**), in good yield. An attempt to effect this copolymerization in dilute pyridine, however, did not yield the expected copolymer. The cyclic diester, cyclic **4d,g**, was obtained instead in very good yield as outlined in Scheme IV. Reactions of **1d** with long-chain bis alcohols such as $HO(CHRCH_2O)_nH$, neat or in dimethylformamide, always gave the corresponding polyesters, which were usually gummy products.

(9) Errede, L. A. U.S. Patent 3 440 228, 1969.
(10) Part 3: Errede, L. A.; Oien, H. T.; Yarian, D. R. *J. Org. Chem.* **1977**, *42*, 12.

Summary and Conclusions

Although reaction of 1 with HNu occurs "abnormally" to give products via pathway A (Scheme II; i.e., interaction is initiated by nucleophilic attack at C-2, the less electropositive center), addition of a small amount of base causes reaction to occur "normally" to give products via pathway B (i.e., interaction is initiated by nucleophilic attack at C-4, the more electropositive center). Thus, the corresponding ester is obtained exclusively, when 1 is made to react with an equivalent amount of ROH and a catalytic amount of ^-OR (Scheme III). The same results are obtained even when HOR is used as the solvent. The 14 examples listed in Table I show that the corresponding ester is always isolated in better than 75% yield, which implies that this may be a general method for synthesis of *o*-(acylamido)benzoate esters.

These results are consistent with the point of view that the observed "abnormal" selectivity for reaction of 1 with HNu (i.e., nucleophilic attack via pathway A, Scheme II) is attributable to formation of 1·$(HNu)_n$ via hydrogen bonding with the heterocyclic nitrogen of 1, which limits subsequent nucleophilic attack to the adjacent electropositive center at C-2 owing to the tether of hydrogen bonding.[9,10] In the presence of Nu^-, which cannot be fettered by hydrogen bonding to either the heterocyclic nitrogen atom or the oxygen atoms of 1, nucleophilic attack occurs "normally" and very rapidly at the more electropositive center C-4 via pathway B.

Experimental Section

General Methods. Melting points were obtained on a Thomas-Hoover melting point apparatus in open capillary tubes and are uncorrected as reported. Elementary analyses were determined by 3M Central Research Analytical Laboratories. The molecular weights were determined by the method of osmometry. The NMR spectra were recorded on Varian XL-100 and Perkin-Elmer R-32 spectrometers. Proton NMR signals are reported as τ values with tetramethylsilane as an internal reference. Infrared spectra were taken on a Perkin-Elmer 137 sodium chloride spectrophotometer, and absorptions are recorded in micrometers.

(1) Reactions of Acetylanthranil (1a: 1, R = CH_3) with Methanol (2a), Ethanol (2b), and Allyl Alcohol (2e) To Give Esters 4a,a, 4a,b, and 4a,e, Respectively (Expts 1–4 and 7). Acetylanthranil (**1a**, 1.8 g) was dissolved in a solution of the alcohol **2** (50 mL) that contained a small amount of base (<0.2 g), preferably the corresponding sodium alkoxide. The solution was then evaporated to dryness within 20 min in an evacuated rotary film evaporator. The residue was washed with water and then recrystallized from heptane to give the corresponding ester, **4**, in the form of colorless crystals in >80% yield as indicated in Table I. The methyl, **4a,a**, and ethyl, **4a,b**, esters of *o*-acetamidobenzoic acid were identified by their corresponding IR spectra and mixture melting point with authentic samples. Allyl *o*-acetamidobenzoate (**4a,e**) was characterized by its melting point (49.0–49.5 °C), IR spectrum (Table I), and elemental analyses. Anal. Calcd for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.98; N, 6.39; mol wt 219.24. Found: C, 66.1; H, 6.0; N, 6.3; mol wt 215.

(2) Reaction of 1a with 2-Propanol (2c) To Give Ester 4a,c, (Expt 5). A solution of **1a** (1.8 g) and 2-propanol (**2c**, 50 mL) that contained a trace amount of sodium isopropoxide was allowed to react at room temperature for 16 h. The solution was separated as described above. The product was isolated as colorless crystals (1.7 g; mp 62–63 °C) which were identified as the isopropyl ester, **4a,c**, of *o*-acetamidobenzoic acid by its IR and NMR spectra.

(3) Reaction of 1a with *tert*-Butyl Alcohol (2d) To Give Ester 4a,d (Expt 6). Acetylanthranil (**1a**, 5 g) was dissolved at room temperature in a solution of *tert*-butyl alcohol (**2d**, 50 mL) and sodium *tert*-butoxide (0.3 g) to give a canary yellow solution. Reaction was allowed to occur at reflux for 3 h. The ester was isolated as described above and then recrystallized from hot ethanol–water solution to give *tert*-butyl *o*-acetamidobenzoate (**4a,d**) in the form of fine colorless needles: 7.2 g; mp 71–72 °C.

The ester was identified by its IR spectrum (Table I) and by molecular weight: calcd for $C_{13}H_{17}O_3N$, 235; found, 236.

(4) Reaction of 1a with Phenol (2f) To Give Ester 4a,f (Expt 8). One pellet of NaOH was added to a solution of acetylanthranil (3 g) in phenol (13.3 g), and the mixture was allowed to react at reflux for 3 h. The excess phenol was removed by distillation at 2 torr [bp 45 °C (2 torr)]. The residue was washed with water and then recrystallized from heptane to give phenyl *o*-acetamidobenzoate (**4a,f**) in the form of colorless crystals: 4.6 g; mp 95–96 °C.

(5) Reaction of 1a with Hexamethylene Glycol (2g) To Give the Bis Ester 4aa,g (Expt 9). A solution of acetylanthranil (5 g, 0.03 mol) in pyridine (25 mL) was added slowly to a solution of hexane-1,6-diol (**2g**; 1.5 g, 0.013 mol) in pyridine (25 mL). The resulting solution was evaporated to dryness in an evacuated rotary evaporator. The residue was leached with warm aqueous $NaHCO_3$ to remove excess **1a** and then recrystallized from ethanol to give hexamethylene bis(*o*-acetamidobenzoate) (**4aa,g**) in the form of colorless crystals: 5.3 g; mp 136–138 °C. The IR spectrum (Table I) and elemental analyses were consistent with that expected for the diester. Anal. Calcd for $C_{24}H_{28}N_2O_6$: C, 65.44; H, 6.41; N, 6.36; mol wt 440. Found: C, 65.6; H, 6.1; N, 6.6; mol wt 435.

(6) Reaction of 1a with Bisphenol-A (2h) To Give the Bis Ester 4aa,h (Expt 10). A solution of acetylanthranil (5.0 g) and 2,2-bis(4-hydroxyphenyl)propane (2h; 2.3 g, 0.01 mol) in pyridine (50 mL) was allowed to react at reflux for 3 h. The solution was then evaporated to dryness as described previously, and the residue was leached with warm $NaHCO_3$ to remove excess **1a**. The IR spectrum (Table I) of the aqueous bicarbonate insoluble residue (5.2 g; mp 222–223 °C) indicated that the major component was the expected bis(*o*-acetamidobenzoate) **4aa,h**.

(7) Reaction of 1a with β-(Diethylamino)ethanol (2k) To Give the Ester 4a,k (Expt 11). A mixture of acetylathranil (1.6 g) and β-(diethylamino)ethanol (1.2 g) was allowed to react at 100 °C for 1 h to give a clear solution that did not solidify at room temperature even after being dried at 0.2 torr overnight at 30 °C. The IR spectrum of the oil (Table I) was consistent with that expected for β-(diethylamino)ethyl *o*-acetamidobenzoate (**4a,k**). The oil was dissolved in anhydrous ether and then precipitated as a gummy mass by addition of anhydrous HCl gas. The gummy mass was digested in fresh ether to remove excess HCl, which gave the salt in the form of a white powder: 3.0 g; mp 144–145 °C. Recrystallization of the powder from hot ethanol–ethyl acetate solution gave the hydrochloride salt, **4a,k**·HCl, in the form of tiny crystals: 2.5 g; mp 146.5–147.0 °C. The IR spectrum (Table I) and elemental analyses were consistent with that expected for the monohydrochloride salt of 2-(dimethylamino)ethyl *o*-acetamidobenzoate. Anal. Calcd for $C_{15}H_{23}O_3N_2Cl$: C, 57.22; H, 7.36; N, 8.90; HCl, 11.58. Found: C, 57.4; H, 7.6; N, 8.9; HCl, 11.7.

(8) Reaction of (Trifluoroacetyl)anthranil (1b: 1, R = CF_3) with Ethanol (2b) To Give Ester 4b,b (Expt 12). (Trifluoroacetyl)anthranil (**1b**) was prepared as described previously.[10] A sample of **1b** (4.4 g) was dissolved at room temperature in ethanol (50 mL) containing a trace amount of NaOEt. The solution was evaporated to dryness immediately thereafter, and the residue was recrystallized from ethanol–water solution to give ethyl *o*-(trifluoroacetamido)benzoate (**4b,b**) in the form of colorless crystals: 4.5 g; mp 80–81 °C. The IR spectrum (Table I) and the neutralization equivalent were consistent with those expected for the ester: neutralization equivalent calcd for $C_{11}H_{10}NO_3F_3$, 262.2; found, 264.

(9) Reaction of Benzoylanthranil (1c) with Hexamethylene Glycol (2g) To Give the Bis Ester 4cc,g, (Expt 13). Benzoylanthranil (mp 122 °C) was prepared essentially as described in the procedure of Anschutz et al.[11] A sample (6 g) was dissolved in a solution of hexamethylene glycol (1.2 g, 0.01 mol) in pyridine (50 mL). Reaction was allowed to occur at reflux for 20 min, and then the solvent was removed by evaporation to dryness in an evacuated rotary evaporator. The residue was leached with hot aqueous $NaHCO_3$ and then recrystallized from ethanol–ethyl acetate solution to give hexamethylene bis(*o*-benzamidobenzoate) (**4cc,g**) in the form of tiny white crystals: 5.5 g; mp 143–144 °C. The IR spectrum and partial elemental analysis were consistent with those expected for this bis ester. Anal. Calcd for $C_{34}H_{32}N_2O_6$: N, 4.96; mol wt 564.7. Found: N, 5.0; mol wt 565.

(10) Reaction of Methylenebis(acetylanthranil) (1d) with Hexamethylene Glycol (2g) To Give the Cyclic Diester 4d,g (Expt 14). Methylenebis(acetylanthranil) (**1d**) was prepared essentially as described by Heller and Fiesselman[12] and as outlined in Scheme IV. Anthranilic acid (mp 144–145 °C) was reacted with formaldehyde in methanol to give *N,N'*-methylene bis(anthranilic acid) (**7**): mp 155.5–156.5 °C; IR (KBr) 3.0, 3.2–4.2, 5.9, 6.3, 6.6, 8.0 μm; 95% yield. Compound **7** was made to undergo rearrangement at 100 °C in concentrated HCl solution to give the hydrochloride salt of bis(2-carboxy-4-aminophenyl)methane (**8**): mp 280 °C dec; IR (Nujol) 3.2–4.2, 5.9, 8.0 μm. The salt was dissolved in a large volume of water and then neutralized with base to pH 6 to give the corresponding hydrochloride-free form of the diamino dicarboxylic acid **8** (mp 256–257 °C; IR (Nujol) 2.9, 3.0, 3.2–4.3, 6.0, 6.3, 7.7, 8.1 μm) in 53% overall yield from anthranilic acid. Compound **8** was converted to methylenebis(acetylanthranil) (**1d**) by cyclodehydration in acetic anhydride at reflux according to the general procedure described earlier.[10] The product was recrystallized from pyridine to give **1d** in the form of tiny light amber platelets: mp 269–271 °C; IR (Nujol) 5.8, 6.2, 8.0 μm. The IR spectrum was consistent with the assigned configuration, which was also supported by its elemental analyses. Anal. Calcd for $C_{19}H_{14}O_4N_2$: C, 68.25; H, 4.19; N, 8.38. Found: C, 68.2; H, 4.2; N, 8.5.

Sodium (0.23 g) was allowed to react at room temperature with hexamethylene glycol (1.1818 g, 0.0100 mol) in pyridine (150 mL) to give a clear solution. Methylenebis(acetylanthranil) (**1d**; 3.343 g, 0.0100 mol) was added, and the reaction was carried out at 70 °C. Although a clear solution was obtained within 1 h, the reaction was allowed to continue overnight to ensure completion. The clear solution was concentrated to 25 mL and then allowed to cool to room temperature. A white precipitate (1.3 g; mp 262–264 °C) separated, and its IR spectrum (Table I) indicated that it was the cyclic diester, **4d,g**, of **1d** and **2g**. The elemental analyses and molecular weight determination were also consistent with those expected for the cyclic diester shown in Scheme IV. Anal. Calcd for $C_{25}H_{28}O_6N_2$: C, 66.34; H, 6.24; N, 6.19; mol wt 452.52. Found: C, 66.3; H, 6.5; N, 6.3; mol wt 454. The mother liquor was evaporated to dryness. The residue was leached with dilute aqueous NaOH. The aqueous extract was acidified with mineral acid to give methylene-5,5'-bis(acetylanthranilic acid) (**9**): 0.2 g; mp 270–272 °C; IR (Nujol) 2.9–4.2, 5.8, 5.9, 6.2, 6.5, 7.7–8.1 μm. The IR spectrum of the alkali insoluble residue (2.9 g; mp 250–260 °C) indicated that the major component was the cyclic diester **4d,g**.

Registry No. **1a**, 525-76-8; **1b**, 16062-71-8; **1c**, 1022-46-4; **1d**, 20006-47-7; **2a**, 67-56-1; **2b**, 64-17-5; **2c**, 67-63-0; **2d**, 75-65-0; **2e**, 107-18-6; **2f**, 108-95-2; **2g**, 629-11-8; **2h**, 80-05-7; **2k**, 100-37-8; **4a,a**, 2719-08-6; **4a,b**, 20628-20-0; **4a,c**, 82679-09-2; **4a,d**, 19849-22-0; **4a,e**, 82679-10-5; **4a,f**, 33163-29-0; **4aa,g**, 82679-11-6; **4aa,h**, 32001-92-6; **4a,k**, 82679-12-7; **4a,k**·HCl, 82679-16-1; **4b,b**, 82679-13-8; **4cc,g**, 82679-14-9; **4d,g**, 82679-15-0; **7**, 61098-02-0; **8**, 7330-46-3; **8**·2HCl, 6268-06-0; **9**, 47548-81-2; anthranilic acid, 118-92-3.

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