was added 0.50 mL of 3-chloropropyl thioacetate. Following the above procedure the thione **3c** was isolated in 70% yield after recrystallization from $CHCl_3$: mp 48–50 °C; IR (KBr) 2910 (w), 1710 (s), 1430 (w), 1388 (m), 1360 (w), 1300 (w), 1250 (w), 1145 (m), 1110 (w), 1060 (s), 1040 (w), 915 (m), 890 (w) cm^{-1}; NMR ($CDCl_3$) δ 2.0 (m, 2 H), 2.1 (s, 3 H), 2.7 (m, 4 H).

1,3,5,7-Tetrathiapentalene-2,6-dithione (4). This compound was prepared following the procedure of Krug et al.[11] The salt cake obtained from the acetonitrile–CS_2 electrolysis solution was dissolved in deaerated ethanol and treated with thiophosgene until the solution was decolorized. An amorphous yellow solid was obtained in quantitative yield based on the stoichiometry of eq 1: mp 208–210 °C dec (compare lit.[17] mp 207–210 °C dec); IR (KBr) 1068 (vs), 959 (m), 900 (w), 776 (m) cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity, assignment) 44 (20.9, CS^+), 64 (7.5, S_2^+), 76 (100, CS_2^+), 88 (85.1, $C_2S_2^+$), 240 (88.1, $C_4S_6^+$), 242 (20.9, M + 2).

1,3,5,7-Tetrathiapentalene-2,6-dione. This compound was prepared by $Hg(OAc)_2$ hydrolysis of **4** following the procedure of Rae.[21] The yellow solid which was obtained by sublimation (90 °C, 0.05 mmHg) was purified further by recrystallization from acetonitrile. Fine white needles were realized in 22% yield: mp 150 °C; IR (KBr) 1727 (m), 1678 (s), 973 (w), 914 (w) cm^{-1}.

Tetrapotassium 2,2′-Bis(1,3-dithiole 4,5-disulfide) (6). A mixture of 100 mL of ethanol, 10 g of KOH, and 1.0 g of 2,2′-bis(1,3,5,7-tetrathiapentalen-6-one), prepared by coupling 1,3,5,7-tetrathiapentalene-2,6-dione,[17] was stirred 10 h under an inert atmosphere. The resulting pink salt was isolated by filtration and washed with a 10-mL portion of EtOH under an argon atmosphere. The salt which darkens upon drying was realized in 90% yield: mp 120 °C; IR (KBr) 1730 (m), 1610 (s), 1440 (s), 1385 (s), 1305 (s), 1140 (m), 1105 (m), 1050 (w), 990 (s), 870 (m), 750 (w), 740 (w), 680 (m), 650 (m) cm^{-1}.

(21) Rae, I. D. *Int. J. Sulfur Chem.* **1973**, *8*, 273.

Exhaustive coulometry was carried out by dissolving 40 mg of this salt in a deaerated solution of 0.1 M TEAP in DMF and oxidizing the mixture at 0.0 V vs. SCE. An *n* value of 4 faradays/mol of **6** was obtained.

2,2′-Bis[4,5-bis[[2-(methylthio)ethyl]thio]-1,3-dithiole] (7b). A mixture of 0.5 g of **6**, 25 mL of DMF, and 7.6 mL of 2-chloroethyl methyl sulfide was stirred for 10 h under argon. A 50-mL portion of water was added slowly with stirring and the mixture extracted with chloroform. After being dried with $MgSO_4$, the brown solution was eluted on neutral alumina with chloroform. The solid was recrystallized from acetonitrile to give golden brown needles in 60% yield: mp 110 °C; IR (KBr) 2960 (w), 2910 (m), 1424 (s), 1320 (w), 1262 (m), 1204 (s), 1126 (w), 1100 (w), 1023 (w), 961 (w), 913 (w), 886 (m), 805 (m), 772 (m), 731 (w), 710 (w), 682 (m) cm^{-1}. Anal. Calcd for $C_{18}H_{28}S_{12}$: C, 34.35; H, 4.49; S, 61.15. Found: C, 34.22; H, 4.64; S, 60.98.

2,2′-Bis[4,5-bis[[3-(thioacetoxy)-1-propyl]thio]-1,3-dithiole] (7c). A mixture of 0.5 g of **6**, 25 mL of DMF, and 3.0 mL of 3-chloropropyl thioacetate was stirred under argon for 10 h. The solution was worked up in the same manner as for **7b** and was eluted on silica gel with a chloroform–ether mixture. The brown solid was realized in 60% yield: mp 95 °C; IR (KBr) 2910 (w), 1710 (s), 1420 (m), 1390 (w), 1300 (w), 1253 (m), 1135 (s), 1107 (s), 948 (m), 874 (w), 766 (w) cm^{-1}. Anal. Calcd for $C_{26}H_{36}O_4S_{12}$: C, 39.16; H, 4.55; S, 48.26. Found: C, 38.97; H, 4.56; S, 48.37.

Acknowledgment. This research was supported by the NSF (Grant No. CHE78-08709) and the University of Tennessee.

Registry No. 3a, 49638-64-4; **3b**, 75949-39-2; **3c**, 75961-52-3; **4**, 64394-46-3; **5**, 75949-40-5; **6**, 75949-41-6; **7b**, 75949-42-7; **7c**, 75949-43-8; CS_2, 74-15-0; methyl iodide, 74-88-4; 2-chloroethyl methyl sulfide, 542-81-4; 3-chloropropyl thioacetate, 13012-54-9; 1,3,5,7-tetrathiapentalene-2,6-dione, 64394-45-2; 2,2′-bis(1,3,5,7-tetrathiapentalen-6-one), 64394-47-4.

Synthesis of Indoles from *N*-(Trifluoroacetyl)-2-anilino Acetals[1]

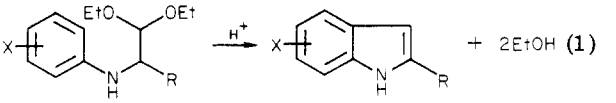
J. Eric Nordlander,* David B. Catalane, Kirtivan D. Kotian, Randall M. Stevens, and Jerome E. Haky

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106

Received July 31, 1980

N-(Trifluoroacetyl)indoles (**3**) are produced in high yield from appropriately ring-substituted *N*-(trifluoroacetyl)-2-anilino acetals (**2**) in boiling trifluoroacetic acid containing excess trifluoroacetic anhydride. Mild saponification provides the free indoles nearly quantitatively. The scope of the reaction is discussed. The ring closure follows solvolytic substitution of a trifluoroacetoxy group for one of the ethoxy groups in **2**. The method has been extended to cyclization of *N*-(trifluoroacetyl)-α-anilinoacetone in hot polyphosphoric acid followed by saponification to yield 3-methylindole.

The biochemical importance of many indole derivatives[2] has spurred continual efforts toward new or improved methods for synthesis of the indole nucleus.[2-4] One early concept for indole construction, eq 1, was acid-catalyzed



cyclization–elimination of 2-anilino acetals,[5] readily

(1) Presented in part at the 178th National Meeting of the American Chemical Society, Washington, DC, Sept 1979; Abstract ORGN 20.

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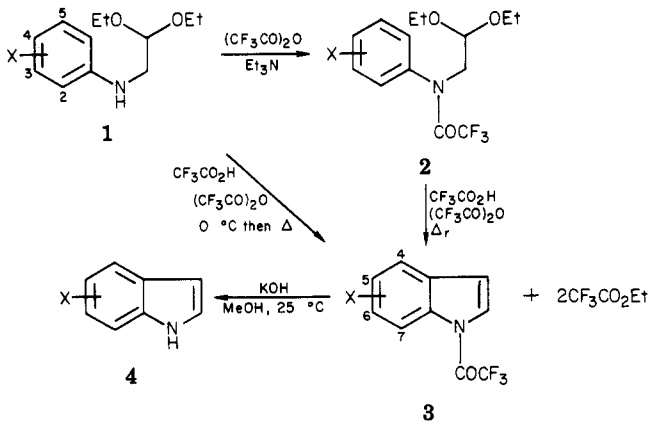
Scheme I



available from the corresponding anilines and α-halo aldehyde acetals. First reports of success by this method[5,6] were found to be unreproducible by succeeding authors, however.[3b,7,8] A thorough reinvestigation by Chastrette[8] in 1962 confirmed the general failure under Brønsted acid conditions, although fair yields of some 2-substituted indoles were realized by using BF_3 as a catalyst in benzene solution. Forbes and co-workers[9] subsequently achieved production of some N-alkyl- (but not N-unsubstituted) indoles from the corresponding anilino acetals by treatment with BF_3–HOAc in trifluoroacetic anhydride.

We report now that the long-envisioned route to N-substituted indoles of eq 1 can be realized in many cases by cyclization following initial trifluoroacetylation of the amino function.[10]

Results and Discussion

Appropriately substituted N-(trifluoroacetyl)-2-anilino acetals (2) produce the corresponding N-(trifluoroacetyl)indoles (3) in high yield in boiling trifluoroacetic acid containing excess trifluoroacetic anhydride[11] (Scheme I).

Table I. N-(Trifluoroacetyl)indoles and Indoles from N-(Trifluoroacetyl)-2-anilinoacetals in Boiling 30% (v/v) $(CF_3CO)_2O$ in CF_3CO_2H (56 °C)

reactant[a] with substituent(s) X in		reaction time, h	product		
				% yield	
1	2		X	3	4
	H	72	H	93	96[b]
	H	148	H	92	
H		72	H	95	
	3,5-Me_2	72	4,6-Me_2	93	97[b]
	3,5-Me_2	80	4,6-Me_2		94[c]
3,4-Me_2		70	5,6-Me_2		76[c]
			4,5-Me_2		10[c]
	3,4-Me_2	75	5,6-Me_2		75[c]
			4,5-Me_2		9[c]
	4-Me	72	5-Me		86[c]
	3-Me	64	6-Me		77[c]
			4-Me		9[c]
	3-MeO	56	6-MeO		59[c]
			4-MeO		6[c]
	2,5-Me_2	71	4,7-Me_2		6[c]
	3-Br	75	6-Br	0	
			4-Br	0	
	4-Br	75	5-Br	0	

[a] Ca. 5 g. [b] Yield from intermediate 3. [c] Yield from reactant 1 or 2.

Table II. Requirement for Excess Trifluoroacetic Anhydride in the Conversion of 2 (X = H)[a] to 3 (X = H)

amt of $(CF_3CO)_2O$ in CF_3CO_2H		isolated yield, %
equiv	vol %	
3.0	6	0
5.0	10	10
10.0	22	78
16.0	30	87
27.0	50	89

[a] 0.50 g.

Saponification at room temperature[12] affords the free indoles 4 essentially quantitatively. Trifluoroacetylation of the anilino acetals 1 can be performed either separately or in situ in the acid medium prior to heating. Our results are presented in Table I.

N-(Trifluoroacetyl)indole (3 (X = H)) was isolated by distillation and identified by matching its ^1H NMR spectrum with that recently reported by Clementi, Linda, and co-workers for the same compound obtained from direct trifluoroacetylation of indole.[13] The 4,6-dimethyl analogue, 3 (X = 4,6-Me_2), was purified by recrystallization and characterized by NMR and elemental analysis. The remaining intermediates 3 were not isolated, but NMR spectra of their concentrates were recorded prior to hydrolysis to the free indoles 4. The latter (in the case of mixtures, the major isomers) were identified by the correspondence of spectroscopic or physical properties with those reported in the literature. Isomeric compositions were estimated from the NMR spectra either before or after deacylation, 3 → 4.

The process is seen to be favorable when the benzene ring is activated for Friedel-Crafts attack ortho to the amino position, the less hindered ortho site being preferred in unsymmetrical cases. Substituents deactivating relative to hydrogen have thwarted the cyclization under the

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(11) For a recent related use of this reaction medium see: Parker, K. A.; Kallmerten, J. *J. Org. Chem.* **1980**, *45*, 2620.

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Table III. ^{1}H NMR Spectra of 2 (X = H) and 5

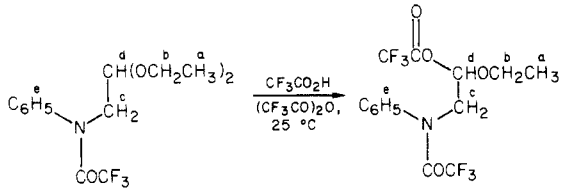
compd	protons e	d	c	b	a
2 (X = H) δ [a]	7.41 (s)	4.87 (t)	3.88 (d)	3.64 (q), 3.60 (q)	1.18 (t)
^3J, Hz		5.5	5.5	7.5	7.5
5 δ [b]	7.51 (m)	6.39 (t)	4.25 (d), 4.22 (d)	3.87 (q), 3.83 (q)	1.26 (t)
^3J, Hz		5.0	5.0	7.0	7.0

[a] For a 15% solution in $CDCl_3$ (Me_4Si). [b] For a 7% solution in CF_3CO_2H plus $(CF_3CO)_2O$ and $CDCl_3$ (1:1:2 by volume) (Me_4Si).

present conditions. The method is also adversely affected by substituents in the prospective indole 7-position (ortho to amino in 1).

The reaction is critically dependent on the presence of excess trifluoroacetic anhydride, as revealed in Table II. We suspect that the ethanol byproduct unless rapidly esterified without water production may divert the synthesis by deacylating 2 or 3. The poor yields experienced in attempted cyclizations to produce 7-substituted *N*-(trifluoroacetyl)indoles (Table I) may be due to facilitated deacylation of the product, 3, when the trifluoroacetyl group is forced out of coplanarity with the pyrrole ring.

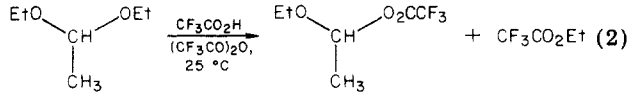
NMR studies showed that cyclization of the *N*-(trifluoroacetyl)anilino acetal 2 is preceded by solvolytic displacement of one of the ethoxy groups. The ^{1}H NMR spectrum of the parent (trifluoroacetyl)amino acetal 2 (X = H) in $CDCl_3$ is given in Table III. The CH_2 protons in the ethoxy groups are anisochronous, as commonly observed in diethyl acetals.[14] On addition of successive small portions of 1:1 (v/v) $(CF_3CO)_2O/CF_3CO_2H$ at room temperature, the original spectrum was incrementally replaced by one corresponding to the ethoxytrifluoroacetoxy derivative 5 (Table III) plus ethyl trifluoroacetate.[15] The



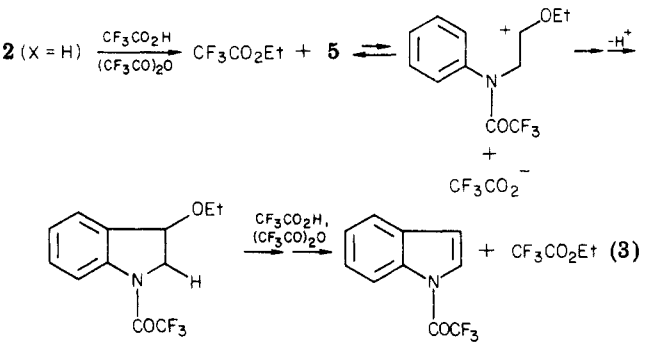
2 5

graded downfield shifts in the spectrum of the new compound are in accord with structure 5, which exhibits anisochronous protons in the two different methylene groups, reflective of the creation of a chiral center.[14] The ^{19}F NMR spectrum of 5, in addition, consists of two well-separated lines of equal intensity. Finally, when a larger sample of 5 thus prepared was evaporated to remove the solvent and remaining reagents and then added to excess KOH in ethanol, the original anilino acetal 1 (X = H) was regenerated as the major product and identified after workup by its NMR spectrum. Intermediate 5 could be distilled [bp 96–97 °C (1 mm)] but decomposed in several hours at room temperature.

Parallel NMR observations were also made for acetaldehyde diethyl acetal itself, eq 2.



The ring closure is thus indicated to be initiated by reversible ionization of 5 (eq 3), a process earlier envisioned by Forbes et al. for acetal cyclizations with BF_3 in trifluoroacetic anhydride.[9]



The success of the present method can be attributed in part to effective reduction of the anilino nitrogen basicity through trifluoroacetylation without severe deactivation of the aromatic ring or acetal function. Unsuccessful earlier efforts to effect the indolization of unprotected anilino acetals with Brønsted acids[3a,b,7,8] assumed the electronic disadvantage of essentially complete initial protonation of the amino group. In addition, the resistance of the (trifluoroacetyl)amino function to acidic cleavage[16] affords protection of products 3 against transformations characteristic of free indoles in strong acid media.[17]

With BF_3 as the acid in warm benzene solvent, Chastrette[8] was able to obtain indoles from free anilino acetals but only if the position α to the acetal function was alkylated. The α-alkyl effect was rationalized as the benefit of steric hindrance against otherwise predominant aldol-type polymerization.[3b,8] For similar cyclizations using BF_3–HOAc in cold trifluoroacetic anhydride, in contrast, Forbes et al. observed an apparent requirement for prior N-alkylation of the starting material, 1, but none for adjacent C-alkylation.[9] It can be speculated that N-trifluoroacetylation of the starting secondary amines in their work may have led to negligibly slow ring closure at the low temperature employed.

The present method has been extended to the preparation of a 3-substituted indole by converting aniline via ketone 6 to skatole (7), eq 4. Cyclization in this case was brought about by heating 6 in polyphosphoric acid at 120 °C after attempted closure in boiling $CF_3CO_2H/(CF_3CO)_2O$ was found ineffectual; the yield for 6 → 7 (two steps) was 64% (0.5-g scale).

We expect the new cyclization to be useful for its provision of *N*-(trifluoroacetyl)indoles as well as the indoles

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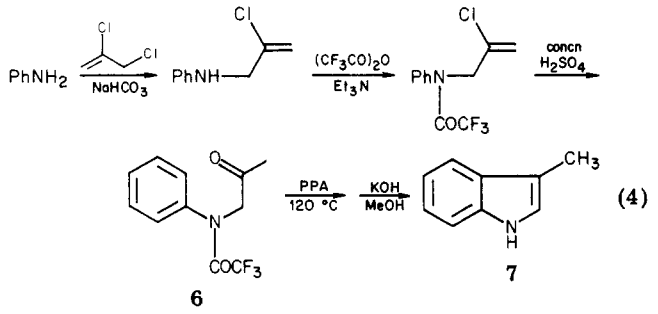

themselves. Compounds **3** should possess distinctive reactivity in both rings, with applicability to the synthesis of more ramified indoles. The direct trifluoroacetylation of indole, by comparison, has been found at best to give **3** (X = H) as one of three significant products.[13]

The indolization of acetals **2** and ketone **6** offers the prospect that a number of other N heterocycles may be accessible by analogous reactions. Further research is in progress.

Experimental Section

General Methods. Capillary melting points and boiling points are uncorrected. ^{1}H NMR spectra were recorded on a Varian A60-A spectrometer using $CDCl_3$ as solvent and Me_4Si as internal standard. ^{19}F NMR spectra were obtained at 94.1 MHz with a Varian XL-100-15 Fourier-transform instrument. Quantitative elemental analyses were performed by Galbraith Laboratories, Inc.

2-Anilino Acetals 1. In a modification of Chastrette's procedure,[8] a solution of 27.9 g (0.30 mol) of aniline, 39.4 g (0.20 mol) of bromoacetaldehyde diethyl acetal, and 25.2 g (0.30 mol) of $NaHCO_3$ in 100 mL of 95% EtOH was boiled under reflux for 96 h. After rotary evaporation of the bulk of the solvent, the product was dissolved in ether, and the resulting solution was washed with water and dried over anhydrous Na_2SO_4. Rotary evaporation of the solvent and vacuum distillation of the residue gave, after a forerun of excess aniline, 30.9 g (0.15 mol, 74%) of colorless 2-anilinoacetaldehyde diethyl acetal (1 (X = H)): bp 97–98 °C (1 mm) [lit.[8] bp 164 °C (18 mm)]; ^{1}H NMR δ 1.17 (t, 6 H, CH_3), 3.19 (d, 2 H, NCH_2), 3.52, 3.59 (both q and 2 H, OCH_2), 4.59 (t, 1 H, $CH(OR)_2$), 6.48–7.35 (m, 5 H, aromatic). The remaining acetals 1 were prepared in the same manner except for that from *m*-methoxyaniline, 1 (X = 3-MeO), where boiling dimethylformamide was used as solvent. Substituents X, yields, and boiling points (pressure) were as follows: 3,5-Me_2, 68%, 128–129 °C (1 mm); 3,4-Me_2, 60%, 139–140 °C (0.5 mm); 4-Me, 66%, 118–120 °C (1 mm); 3-Me, 64%, 116–119 °C (1 mm) [lit.[8] bp 164–165 °C (16 mm)]; 3-MeO, 65%, 152–156 °C (3 mm); 2,5-Me_2, 56%, 126–128 °C (1 mm); 3-Br, 62%, 129–132 °C (0.5 mm); 4-Br, 54%, 131-133 °C (0.5 mm). These compounds had ^{1}H NMR spectra within the following limits: δ 1.16 ± 0.03, 3.17 ± 0.03, 3.58 ± 0.04, 4.61 ± 0.04, 6.4–7.4 (see above for assignments).

***N*-(Trifluoroacetyl)-2-anilino Acetals 2.** To a magnetically stirred solution of 7.3 g (36 mmol) of 2-anilino acetal 1 (X = H) and 4.2 g (42 mmol) of triethylamine in 50 mL of dry hexane cooled in an ice–water bath was added dropwise 8.4 g (40 mmol) of trifluoroacetic anhydride. The mixture was stirred at room temperature for 1 h and then shaken with a sizeable volume of cold water plus 50 mL of ether in a separatory funnel. The organic layer was washed with water and dried over anhydrous $MgSO_4$. Distillation gave 10.6 g (35 mmol, 97%) of pale yellow 2 (X = H), which darkened progressively on being allowed to stand: bp 97–100 °C (0.5 mm); ^{1}H NMR, Table III. Saponification of a sample of the product with KOH in MeOH regenerated the starting acetal, 1 (X = H). The other *N*-(trifluoroacetyl)anilino acetals **2** were prepared likewise. Substituents X, yields, and melting or boiling points (pressure) were as follows: 3,5-Me_2, 97%, 37.0–38.5 °C (after sublimation and recrystallization from hexane at –20 °C); 3,4-Me_2, 95%, 142–144 °C (1 mm); 4-Me, 96%, 136–138 °C (1.5 mm); 3-Me, 94%, 123–125 °C (1 mm); 3-MeO, 95%, 170–172 °C (4 mm); 2,5-Me_2, 96%, 131–134 °C (1 mm); 3-Br, 93%, 136–137.5 °C (1 mm); 4-Br, 94%, 142–143 °C (1.5 mm). These compounds had ^{1}H NMR spectra within the following limits: δ 1.18 ± 0.02, 3.60 ± 0.04, 3.84 ± 0.04, 4.84 ± 0.03, 6.9–7.7 (see Table III for assignments).

Anal. Calcd for $C_{16}H_{22}F_3NO$ (2, X = 3,5-Me_2): C, 57.82; H, 6.37. Found: C, 57.68; H, 6.54.

***N*-(Trifluoroacetyl)indoles 3.** To 100 mL of a 30% (v/v) solution of freshly distilled $(CF_3CO)_2O$ in CF_3CO_2H heated under reflux (56 °C) under a N_2 atmosphere was added dropwise 5.0 g (16 mmol) of *N*-trifluoroacetyl acetal **2** (X = H), and heating was continued for 72 h. The excess anhydride, acid, and product CF_3CO_2Et were removed by distillation at 60 mm through a Vigreux column leading to a dry ice condenser. (The anhydride can be purified from this mixture by fractional distillation; alternatively, the mixture can be fully converted to the useful[18] CF_3CO_2Et by reaction with ethanol in the presence of sulfuric acid.[19]) Distillation of the residue produced 3.2 g (15 mmol, 93%) of *N*-(trifluoroacetyl)indole (**3** (X = H)), bp 58–59 °C (0.6 mm) [lit.[13] bp 118–120 °C (20 mm)], identified by the match of its ^{1}H NMR spectrum with that reported by Clementi, Linda, et al.[13]

From **2** (X = 3,5-Me_2) was prepared likewise crystalline **3** (X = 4,6-Me_2) in 93% yield: mp 76–78 °C (recrystallized from hexane at –20 °C); ^{1}H NMR δ 2.45 (s, 6 H, CH_3, CH_3), 6.69 (d, 1 H, J = 4.0 Hz, H(3)), 6.98 (s, 1 H, H(5)), 7.37 (m, 1 H, H(2)), 8.10 (s, 1 H, H(7)). The NMR assignments were deduced from the spectra of other (trifluoroacetyl)indoles **3** having particular positions substituted and were in accord with those made by Clementi, Linda, and co-workers[13] for the parent amide, **3** (X = H). Anal. Calcd for $C_{12}H_{10}F_3NO$: C, 59.75; H, 4.18. Found: C, 59.89; H, 4.22.

N-(Trifluoroacetyl)indole could also be conveniently produced from 2-anilinoacetal 1 (X = H) without discrete prior acylation. To 50 mL of 50% (v/v) $(CF_3CO)_2O$ in CF_3CO_2H at 0 °C under nitrogen was added 5.0 g (24 mmol) of 1 (X = H). After 30 min the cold mixture was diluted with 40 mL of CF_3CO_2H and boiled under reflux for 72 h. Distillation as before gave 4.8 g (23 mmol, 95%) of **3** (X = H).

The *N*-(trifluoroacetyl)indoles have distinctive NMR features, H(3) characteristically appearing as a clean doublet ($J \approx 4$ Hz) at $\delta \sim 6.7$ and H(7) as an isolated multiplet in the region δ 8.0–8.6. Isolation of these intermediates beyond **3** (X = H) and **3** (X = 4,6-Me_2) was not undertaken, however.

Indoles 4. Treatment of 3.0 g (14 mmol) of *N*-(trifluoroacetyl)indole (**3** (X = H)) with 40 mL of 5% methanolic KOH at room temperature overnight, rotary evaporation of the bulk of the methanol, standard extractive workup with ether, and distillation (1 mm) gave 1.6 g (13.5 mmol, 96%) of indole: mp 50–51.5 °C (lit.[20] mp 52 °C); ^{1}H NMR in agreement with that recorded by Pouchert and Campbell.[21]

The other indoles in Table I were obtained similarly from precursors **3**, except for purification generally by recrystallization (typically from hexane at –20 °C) instead of distillation. The end products were identified by matching the melting points of the free indoles or derived picrates[22] or both with values reported in the literature. All of the synthesized indoles exhibited ^{1}H NMR spectra consistent with the anticipated structures. Substituent(s) X, indole melting point or boiling point (pressure), picrate melting point, and ^{1}H NMR chemical shifts were as follows: 4,6-Me_2, 104–106 °C (1 mm) [lit.[23] 90–95 °C (0.4 mm)], 171–173 °C (lit.[23] 169 °C), δ 2.35, 2.41 (each s, 3 H, CH_3), 6.28–6.82 (m, 4 H, aromatic), 7.00 (br s, 1 H, NH); 5,6-Me_2, 57–59 °C (apparently depressed by the 4,5-Me_2 minor isomer; lit.[23] 64 °C), 153–154.5 °C (lit.[23] 154.5 °C), δ 2.35 (s, 6 H, CH_3), 6.31–6.54 (m, 1 H, aromatic), 6.85–7.13 (m, 2 H, aromatic), 7.30–7.45 (s, 1 H, aromatic), 7.72

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(br s, 1 H, NH); 5-Me, 59–60 °C (lit.[24] 58–59 °C), 152–153 °C (lit.[25] 151–154 °C), δ 2.36 (s, 3 H, CH_3), 6.30–6.49 (m, 1 H, aromatic), 6.81–7.49 (m, 4 H, aromatic), 8.6 (br s, 1 H, NH); 6-Me, 28–29.5 °C (lit.[4m] 29–30.5 °C), δ 2.36 (s, 3 H, CH_3), 6.38–6.46 (m, 1 H, aromatic), 6.70–7.50 (m, 4 H, aromatic), 8.20 (br s, 1 H, NH); 6-MeO, 91–92 °C (lit.[4f] 88–90 °C), 122–123 °C (lit.[26] 118–120 °C), δ 3.90 (s, 3 H, CH_3O), 6.48–6.65 (m, 1 H, aromatic), 6.77–7.79 (m, 4 H, aromatic), 8.09 (br s, 1 H, NH); 4,7-Me_2, 100–101 °C (lit.[23] 101–102 °C), ^{1}H NMR in agreement with that reported by Dalton and Teitei.[27]

Identification of Intermediate Ester 5. To a solution of ~10 mg of *N*-(trifluoroacetyl)-2-anilino acetal **2** (X = H) in 0.4 mL of $CDCl_3$ (1% Me_4Si) in a standard 5-mm NMR tube was added a few drops of 1:1 (v/v) $(CF_3CO)_2O$–CF_3CO_2H. The tube was capped and shaken, and after 10 min the ^{1}H NMR spectrum was recorded. In addition to the familiar signals from the remaining **2** (X = H) a new set of absorptions was exhibited with comparatively downfield chemical shifts. Further treatment with the anhydride–acid reagent (cumulative volume 0.4 mL) caused disappearance of the reactant and sharpening of the product spectrum (Table III). The latter was in agreement with replacement of one of the original ethoxy groups by trifluoroacetoxy to give structure **5** (see text) together with 1 equiv of ethyl trifluoroacetate[15] (δ 1.40, 4.50 under present conditions). The ^{19}F NMR spectrum of the same solvolysis product consisted of two sharp peaks of equal intensity at −0.26 and −8.73 ppm relative to the internal CF_3CO_2H reference, accompanied by signals for the anhydride and CF_3CO_2Et at 0.38 and −0.05 ppm, respectively, identified by additions of authentic materials.

To 10 mL of neat $(CF_3CO)_2O$ in a 250-mL, round-bottomed flask cooled in an ice bath was added dropwise ~0.5 g of **2** (X = H) with thorough swirling. After 5 min most of the excess anhydride and the CF_3CO_2Et product were removed by rotary evaporation, and the residual liquid was identified as **5** by ^{1}H NMR. Addition of the product to 30 mL of a stirred 5% solution of KOH in EtOH followed after 30 min by rotary evaporation of the bulk of the solvent, standard ether–water extractive workup, drying ($MgSO_4$), and rotary evaporation of the ether left a crude product identified by its ^{1}H NMR spectrum as predominantly anilino acetal **1** (X = H).

A sample of **5** was purified by short-path vacuum distillation [bp 96–97 °C (1 mm)] although the neat product darkened in several hours at room temperature.

Treatment of a $CDCl_3$ solution (Me_4Si) of acetaldehyde diethyl acetal with $(CF_3CO)_2O$–CF_3CO_2H produced a transformation analogous to that of **2** (X = H). The reactant CH signal at δ 4.71 (q, ^3J = 5.5 Hz) and attached CH_3 signal at δ 1.28 (d, ^3J = 5.5 Hz) were replaced by new absorptions at δ 6.14 and 1.55 (same multiplicities, ^3J = 5.0 Hz), respectively, indicating product $CH_3CH(OC_2H_5)(O_2CCF_3)$. Decomposition in solution ensued during 15 min, however.

3-Methylindole (7). A solution of 2.5 g (22.5 mmol) of 2,3-dichloropropene, 2.8 g (30 mmol) of aniline, and 2.5 g (30 mmol) of $NaHCO_3$ in 50 mL of 95% EtOH under N_2 was boiled under reflux for 3 days. Rotary evaporation, ether extraction, water washing, drying ($MgSO_4$), and distillation gave 2.68 g (16 mmol, 71%) of 3-anilino-2-chloropropene: bp 116–118 °C (2 mm); ^{1}H NMR δ 3.80 (d, J = 1.5 Hz, 2 H, NCH_2), 3.95 (s, 1 H, NH), 5.30 (m, 2 H, $=CH_2$), 6.40–7.45 (m, 5 H, arom). This compound was trifluoroacetylated in 88% yield as described above for **2** (X = H): bp 94–96 °C (2 mm); ^{1}H NMR δ 4.57 (s, 2 H, NCH_2), 5.30 (dd, 2 H, $=CH_2$), 7.35 (m, 5 H, aromatic). The resultant $PhN(COCF_3)CH_2CHCl{=}CH_2$ (2.00 g, 7.6 mmol) was added to 30 mL of concentrated H_2SO_4, and the mixture was stirred for 2 h and then poured over ice. The crude solid product was collected by filtration, sublimed under vacuum, and recrystallized from hexane at −20 °C to give 0.94 g (3.8 mmol, 54%) of *N*-trifluoroacetyl ketone **6**: mp 66–67 °C; ^{1}H NMR δ 2.20 (s, 3 H, CH_3), 4.61 (s, 2 H, CH_2), 7.51 (s, 5 H, aromatic). Anal. Calcd for $C_{11}H_{10}F_3NO_2$: C, 53.88; H, 4.11. Found: C, 53.72; H, 4.12.

To 20 mL of stirred polyphosphoric acid prepared from 12 mL of 85% orthophosphoric acid and 20 g of P_2O_5 as described by Dev et al.[28] and heated to 120 °C was added 0.47 g (1.91 mmol) of **6**. After 40 min the dark reaction mixture was poured onto crushed ice and extracted with ether. The residual crude product after rotary evaporation of the solvent was treated with 10 mL of 5% KOH in MeOH at room temperature overnight. Rotary evaporation of the methanol, extraction into ether, drying (K_2CO_3), solvent removal and vacuum sublimation gave 1.61 g (1.23 mmol, 64%) of skatole (**7**): mp 96–98 °C (lit.[29] mp 95 °C); ^{1}H NMR, same as that recorded by Pouchert and Campbell.[30]

Acknowledgment. Support of this work from National Science Foundation Grant CHE75-04284-A02, a grant from the Dreyfus Foundation for undergraduate research, financial aid to D.B.C. from the Cleveland Chemical Association Scholarship Fund, and a generous gift of trifluoroacetic acid from Halocarbon Products Corp. are gratefully acknowledged.

Registry No. **1** (X = H), 22758-34-5; **1** (X = 3,5-Me_2), 75934-26-8; **1** (X = 3,4-Me_2), 75934-27-9; **1** (X = 4-Me), 75934-28-0; **1** (X = 3-Me), 75934-29-1; **1** (X = 3-MeO), 32431-44-0; **1** (X = 2,5-Me_2), 75934-30-4; **1** (X = 3-Br), 75934-31-5; **1** (X = 4-Br), 75934-32-6; **2** (X = H), 75934-33-7; **2** (X = 3,5-Me_2), 75934-34-8; **2** (X = 3,4-Me_2), 75934-35-9; **2** (X = 4-Me), 75934-36-0; **2** (X = 3-Me), 75934-37-1; **2** (X = 3-MeO), 75934-38-2; **2** (X = 2,5-Me_2), 75934-39-3; **2** (X = 3-Br), 75934-40-6; **2** (X = 4-Br), 75934-41-7; **3** (X = H), 62615-78-5; **3** (X = 4,6-Me_2), 75934-42-8; **4** (X = H), 120-72-9; **4** (X = 4,6-Me_2), 75948-77-5; **4** (X = 5,6-Me_2), 30877-30-6; **4** (X = 4,5-Me_2), 27866-47-3; **4** (X = 5-Me), 614-96-0; **4** (X = 6-Me), 3420-02-8; **4** (X = 4-Me), 16096-32-5; **4** (X = 6-MeO), 3189-13-7; **4** (X = 4-MeO), 4837-90-5; **4** (X = 4,7-Me_2), 5621-17-0; **5**, 75948-78-6; **6**, 75934-43-9; **7**, 83-34-1; aniline, 62-53-3; bromoacetaldehyde diethyl acetal, 2032-35-1; 2,3-dichloropropene, 78-88-6; 3-anilino-2-chloropropene, 15332-67-9; $PhN(COCF_3)CH_2CHCl{=}CH_2$, 75934-44-0.

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