11-(2-Nitro-2-propyl)-6-chloro-11*H*-dibenzo[*b*,*e*]azepine (4c).—A 10.0-mmol (2.94 g) sample of **3c**[5] was added to a suspension of 20 mmol (4.16 g) of PCl_5 in CCl_4 (50 ml); the mixture was heated to the boiling point and maintained under reflux for 2 hr. Solvent was removed *in vacuo*, and the residual oil was heated at 65° for 2 hr at 0.5 mm to remove other volatile materials. The oil was dissolved in CH_2Cl_2 (10 ml), the solution was filtered, and the filtrate was diluted with 20 ml of CCl_4, heated to the boiling point, and concentrated to a volume of 20 ml. A 10-ml portion of CCl_4 was added and the solution was reconcentrated to 20 ml; this procedure was repeated one additional time. Crystallization was initiated only with considerable difficulty; after 12 hr at room temperature, 2.1 g of crystals had been deposited. A second crystallization afforded 1.29 g (41%) of analytically pure product: mp 124–129°; ir (KBr) 1540, 760, 1645, 940, 1350, 1375, and 1400 cm^{-1}; nmr (CCl_4) δ 1.45 (6 H, s, CH_3), 4.7 (1 H, s, $CHCMe_2NO_2$), and 7–8 ppm (8 H, m, aromatic).

Anal. Calcd for $C_{17}H_{15}N_2O_2Cl$: C, 64.85; H, 4.81; N, 8.90; Cl, 11.27. Found: C, 64.69; H, 4.78; N, 9.01; Cl, 11.37.

Tosylate of 3c.—A 3.0-mmol (889 mg) sample of **3c**[5] was added to a suspension of 3.34 mmol of oil-free NaH in THF (50 ml), and the mixture was warmed briefly at the boiling point prior to the addition of a solution of 3.0 mmol of *p*-toluenesulfonyl chloride in a small volume of THF. The reaction mixture was maintained at the boiling point for 12 hr prior to solvent removal (*in vacuo*). The residue was dissolved in benzene (50 ml) and the solution was washed with two 100-ml portions of water, dried (Na_2SO_4), and concentrated to a residue. The residue was crystallized from CH_2Cl_2–EtOH: yield 870 mg (64%); mp 184–187° dec; ir (KBr) 1375, 1195, and 1180 ($ArSO_3$–) and 1595 cm^{-1} ($Ar_2C{=}N$–); nmr (acetone-d_6) δ 1.2 [6 H, s, $C(CH_3)_2NO_2$], 2.4 (3 H, s, $ArCH_3$), 4.8 (1 H, s, $CHCMe_2NO_2$), and *ca.* 8.5 ppm (12 H, m, aromatic).

Anal. Calcd for $C_{24}H_{22}N_2O_5S$: C, 63.98; H, 4.92; N, 6.22; S, 7.12. Found: C, 63.78; H, 4.91; N, 6.32; S, 7.03.

5-(2-Dimethylaminoethyl)-11-dicarbethoxymethyl-5,6-dihydro-11*H*-6-oxodibenzo[*b*,*e*]azepine (6a).—A 25.0-mmol (9.19 g) sample of **5a** was added to a suspension of 62.5 mmol of oil-free NaH in 125 ml of DMSO, and the mixture was stirred at room temperature for 1 hr prior to the addition of a suspension of 37.5 mmol (3.6 g) of 2-dimethylaminoethyl chloride hydrochloride in 50 ml of DMSO. The reaction mixture was stirred for 3 hr and poured into 600 ml of water. An orange semisolid separated; the supernatant was rendered strongly alkaline by the addition of 10 ml of 10 *N* NaOH, and was extracted with five 70-ml portions of CCl_4. The semisolid was dissolved in the combined extract and the solution was washed, dried (Na_2SO_4), and concentrated *in vacuo;* the resulting oil was purified by chromatography on silica gel. Elution with 10% EtOH–CH_2Cl_2 afforded (after solvent removal) 1.17 g (12.7%) of recovered **5a**. Elution with 25% EtOH–CH_2Cl_2 provided (after solvent removal *in vacuo*) an oil which could be induced to crystallize from toluene with considerable difficulty, yield 2.94 g, mp 134–154°. Two recrystallizations from PhMe afforded 2.06 g (21.5% conversion) of product: mp 142–146°; ir (KBr) 1640, 1730, 1750, 1370, 1290–1330, 1250, and 1445 cm^{-1}; nmr (acetone-d_6) δ 0.98 and 1.03 (6 H, two triplets, J = 7 Hz, CH_2CH_3),[17] 3.0 [6 H, s, $N(CH_3)_2$], 3.6–5.0 [10 H, m, CH_2CH_3, $CHCH(CO_2Et)_2$, and $CH_2CH_2NMe_2$], and 7.0–8.0 ppm (8 H, m, aromatic).

A 4.7-mmol (2.05 g) sample of **6a** was dissolved in EtOH (15 ml), and hydrobromic acid (4.7 mmol, 0.53 ml) was added. Dilution with an equal volume of Et_2O and cooling at −15° for 12 hr caused the crystallization of the HBr salt: yield 1.90 g (78%); mp 162.5–165°; mass spectrum[18] *m/e* 438.2143 (calcd for $C_{25}H_{31}N_2O_5Br$ − HBr: 438.2154).

Anal. Calcd for $C_{25}H_{31}N_2O_5Br$: C, 57.81; H, 6.02; N, 5.39; Br, 15.38. Found: C, 58.36; H, 6.25; N, 5.43; Br, 15.14.

5-(2-Dimethylaminoethyl)-11-(2-nitro-2-propyl)-5,6-dihydro-11*H*-6-oxodibenzo[*b*,*e*]azepine (6c).—A solution of **5c** (6.0 mmol, 1.78 g) in DMSO (15 ml) was added to a suspension of 6.4 mmol of oil-free NaH in 10 ml of DMSO. After 1.5 hr a suspension of 9.9 mmol of oil-free NaH in a solution of 2-dimethylaminoethyl chloride hydrochloride (9.0 mmol, 1.30 g) in 10 ml of DMSO was added, and stirring was continued for an additional 2.5 hr. The mixture was poured into 250 ml of water and the suspension was extracted into CH_2Cl_2 (five 30-ml portions). The extract was washed with a 200-ml portion of water, and basic substances were extracted into 0.15 *N* HCl (three 40-ml portions). The aqueous solution was made strongly alkaline by the addition of concentrated NaOH and the free amine was extracted into CCl_4 (five 30-ml portions). Upon concentration of the CCl_4 extract to a small volume and cooling for several hours at −15°, 1.066 g of product crystallized. Recrystallization from CH_2Cl_2–EtOH afforded 977 mg (44%) of **6c**, mp 157–162°. The analytical sample was obtained by repeated recrystallizations from CH_2Cl_2–EtOH, and melted at 160–162°: ir (KBr) 1630, 1530, 1380, 1455, 1323, and 1400 cm^{-1}; nmr ($CDCl_3$) δ 1.6 [6 H, s, $C(CH_3)_2NO_2$], 2.4 [6 H, s, $N(CH_3)_2$], 2.7–4.4 (4 H, m, $CH_2CH_2NMe_2$), 4.4 (1 H, s, $CHCMe_2NO_2$), and 7.0–8.0 ppm (8 H, m, aromatic); mass spectrum[18] *m/e* 367.1901 (calcd for $C_{21}H_{25}N_3O_3$: 367.1896).

Anal. Calcd for $C_{21}H_{25}N_3O_3$: C, 68.64; H, 6.86; N, 11.44. Found: C, 68.14; H, 6.77; N, 11.43.

Registry No.—**3a**, 29925-32-4; **3b**, 29925-33-5; **3c**, 29925-34-6; **3c** tosylate, 37387-62-5; **4c**, 37387-63-6; **5a**, 37387-64-7; **5b**, 37387-65-8; **5c**, 37387-66-9; **6a**, 37387-67-0; **6a**, 37387-67-0; **6a** HBr, 37387-68-1; **6c**, 37387-69-2.

(18) Exact mass measurements were obtained by the peak-matching technique by Mr. J. Carter Cook using a MAT 731 high-resolution mass spectrometer and data-processing equipment provided by NIH grants CA 11388 and GM 16864, from the National Cancer Institute and the National Institute of General Medical Studies, respectively.

4,5,6,7-Tetrafluoroindole

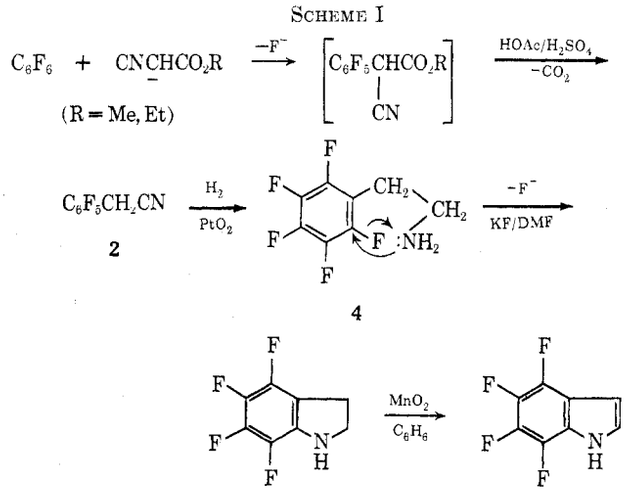
ROBERT FILLER,* SARAH M. WOODS,[1] AND ALLEN F. FREUDENTHAL[2]

Department of Chemistry, Illinois Institute of Technology, Chicago, Illinois 60616

Received August 17, 1972

We wish to report a convenient synthesis of 4,5,6,7-tetrafluoroindole (**1**) by a vastly improved five-step sequence starting with hexafluorobenzene (Scheme I).

SCHEME I



Previous routes to **1** have suffered from serious drawbacks, *e.g.*, tedious multistep procedures[3] from readily

(1) Abstracted, in part, from the Ph.D. Thesis of S. M. W., May 1972.
(2) NSF Undergraduate Research Participant, summer 1971.
(3) V. P. Petrov, V. A. Barkhash, G. S. Schegoleva, T. D. Petrova, T. I. Savchenko, and G. G. Yakobson, *Dokl. Akad. Nauk, SSSR*, **178**, 864 (1968).

available starting materials, low and nonreproducible yields of pentafluorophenylacetonitrile (2), and difficulties encountered in the final aromatization step.

The key intermediate in our sequence is the nitrile 2, which is readily prepared in one extended step by nucleophilic reaction of hexafluorobenzene with the anion of methyl (or ethyl) cyanoacetate.[4] While the resulting cyano ester is isolable (80% yield), the crude product may be selectively hydrolyzed *in situ* to the nitrile by heating under reflux with 50% acetic acid containing a small amount of concentrated sulfuric acid.[5] The yield of 2 from hexafluorobenzene is 60–70%.

The previously described[6] route to 2 involves the prior preparation of $C_6F_5CH_2X$ (X = Cl, Br), followed by S_N2 displacement of X^- by cyanide ion. Earlier reports have apparently failed to note that this reaction is *always* accompanied by an undesirable side reaction to yield 15–20% of 2,3-bis(pentafluorophenyl)propionitrile, $C_6F_5CH_2C(CN)HC_6F_5$ (3). Details of the latter reaction will be reported separately.

Compound 2 was catalytically reduced (PtO_2) to 2-pentafluorophenylethylamine (4), which was isolated (81%) as its hydrochloride to obviate the facile intermolecular nucleophilic reaction of the free amine with the pentafluorophenyl ring.[7] Cyclization of the amine 4, which was generated from its hydrochloride as needed, was accomplished by heating with potassium fluoride in dimethylformamide to give a 70% yield of the indoline 5.[3] The indoline was then smoothly aromatized to the indole 1, mp 91–92°, in 82% yield, on treatment with activated manganese dioxide in cold benzene.[8] A host of other reagents, including palladium on charcoal,[3] were found to be much less effective.

The accessibility of 4,5,6,7-tetrafluoroindole has permitted the exploration of the chemical reactivity of this interesting heterocycle. These results will be reported in due course.

Experimental Section

Ethyl α-Cyanopentafluorophenylacetate.—An adaptation of a method employed by Kalir and Pelah[5] was used. A mixture of 650 ml of reagent grade dimethylformamide and 140 g (1.0 mol) of anhydrous potassium carbonate was heated in a 2-l., four-neck flask equipped with a mechanical stirrer, addition funnel, thermometer, and condenser. Water was allowed to flow through the condenser after the temperature of the mixture reached 152–154°, and 113 g (1.0 mol) of ethyl cyanoacetate was added dropwise rapidly without further heating. The temperature of the bright orange mixture was allowed to drop to 110–120° and was maintained within this range while 186 g (1.0 mol) of hexafluorobenzene was added dropwise. The deep brown mixture was stirred for 3 hr after addition was complete, then poured into 3 l. of ice-cold water and acidified with 20% sulfuric acid until all of the potassium carbonate dissolved. A dark brown organic layer settled to the bottom of the beaker. After cooling for 2 hr, the top layer was decanted and discarded. The organic layer was dissolved in ether, washed with water and then with sodium bicarbonate, and dried over anhydrous $MgSO_4$. After removal of the ether on a rotary evaporator, the residue weighed 223 g (80% crude yield). An analytical sample was prepared by dissolving about 2 g of this crude substance in a minimum amount of hot 95% ethanol. Hexane was added until the mixture became turbid. Crystallization occurred when the mixture was cooled in Dry Ice. The solid was filtered on a Büchner funnel and transferred quickly to a sublimator. Triple sublimation at 30° (1.0–0.7 Torr) produced white needles: mp 32° (uncorrected); ir 2920 and 2985 (s, CH_3), 2260 (s, C≡N), 1760 (s, C=O), 1650, 1620, 1570 cm^{-1} (s, aromatic); pmr (CCl_4) δ 5.03 (s, 1, CH) 4.33 (q, 2, CH_2) 1.35 (t, 3, CH_3).

Anal. Calcd for $C_{11}H_6F_5NO_2$: C, 47.27; H, 2.16; N, 5.01. Found: C, 47.06; H, 2.02; N, 4.82.

2,3,4,5,6-Pentafluorophenylacetonitrile (2).—Ethyl α-cyanopentafluorophenylacetate (0.5 mol, 140.5 g) was refluxed for 12 hr with 350 ml of 50% acetic acid containing 12.5 ml of concentrated sulfuric acid. After the mixture was cooled to room temperature, it was diluted with an equal volume of water and stirred, and the viscous, dark organic layer settled to the bottom of the flask. The mixture was chilled in an ice bath, the top layer was decanted until the remaining mixture consisted mostly of the dark organic layer, which was transferred to a separatory funnel, and the remaining water layer was removed. The organic layer was dissolved in ether, washed with water and sodium bicarbonate, and finally dried over anhydrous $MgSO_4$. Distillation through a 10-in. jacketed Vigreux column gave 98.0 g (70%) of a colorless liquid: bp 105–107° (8 Torr); ir 2925 and 2900 (s, CH_2) 2260 (w, C≡N) 1660 (s, aromatic), 1540 (s, C_6F_5), and 1160 (s, CF); pmr δ 3.97 (s, fine structure).

The spectra of this substance were identical with those obtained for an autheutic sample of the nitrile, although the boiling point of the material prepared by the present method was slightly higher than that reported earlier [bp 107–111° (17 Torr[6])].

This compound was reduced over PtO_2[3] and the resulting amine hydrochloride was converted to the free amine, which was cyclized to the indoline, mp 60° (lit.[3] mp 60–61.5°).

Aromatization of 4,5,6,7-Tetrafluoroindoline to 4,5,6,7-Tetrafluoroindole.—A modification of a method described by Jansen, Johnson, and Surtees was employed.[8] To 4.5 g (23.5 mmol) of the tetrafluoroindoline in a round-bottom, one-neck flask was added 190 ml of reagent-grade benzene which was predried over sodium and filtered and chilled to about 10°. Then 4.0 g of Linde Type 4A Molecular Sieves and 22.0 g of activated MnO_2 were added.[9] The mixture was shaken on a wrist-action shaker for 60 hr, during which time the temperature was not allowed to rise above 22°. After the mixture had been filtered on a Büchner funnel using Celite, the solid residue was transferred to a Soxhlet apparatus and extracted with 300 ml of dry benzene for 7 hr. The filtrate and liquid from the extraction were combined and the benzene was removed on a rotary evaporator. The residual brown oil was diluted with about 3 ml of dry benzene and transferred to a 2 ft × 1.2 in. (o.d.) chromatography column packed with 25 g of neutral alumina in practical-grade hexane. The contents of the column were eluted first with 250 ml of hexane, then with 50:50 hexane–diethyl ether, and finally, with 100% ether. The hexane and hexane–diethyl ether fractions were concentrated on the rotary evaporator to yield a material melting at 83–90°. Sublimation at 60° (0.7–1.5 Torr) yielded 3.7 g (82%) of a white solid: mp 91–92.5° (this melting point is identical with that reported for the pure indole[3]); ir 3420 (vs, NH), 3100 (s, CH), 1540, 1600, 1660, and 1490 (aromatic ring), 1500, 1130, and 1000 cm^{-1} (s, CF); pmr δ 8.37 (s, broad, 1, NH), 7.17 (m, 1, CH), 6.57 (m, 1, CH). The solid obtained from the 100% ether eluate contained a mixture of indole, unreacted indoline, and some unidentified materials whose melting points were variable and ranged from 110 to 130°.

Registry No.—1, 16264-67-8; 2, 653-30-5; ethyl α-cyanopentafluorophenylacetate, 2340-87-6.

(4) W. P. Norris, *J. Org. Chem.*, **37**, 147 (1972), has recently reported an analogous reaction with octafluorotoluene.

(5) A. Kalir and Z. Pelah, *Israel J. Chem.*, **4**, 155 (1966).

(6) A. K. Barbour, M. W. Buxton, P. L. Coe, R. Stephens, and J. C. Tatlow, *J. Chem. Soc.*, 808 (1961).

(7) W. L. White and R. Filler, *J. Chem. Soc. C*, 2062 (1971).

(8) A. B. A. Jansen, J. M. Johnson, and J. R. Surtees, *J. Chem. Soc., Suppl. 1*, 5573 (1964).

(9) J. Attenburrow, J. H. Cameron, R. M. Evans, A. B. A. Evans, and T. Walker, *J. Chem. Soc.*, 1104 (1952).