moved with a rotovapor apparatus to give a yellowish oily residue which was chromatographed on a small column of silica gel (100 g) in hexane, affording 15.8 g (81%; 98% based on unrecovered 3-methoxyphenol) of 8 and 2.1 g of recovered 3-methoxyphenol. A sample obtained by vacuum distillation had bp 144–145 °C (16 mm); n^{25}_D 1.5591 (lit.[9] bp 142–144 °C (15 mm); n^{25}_D 1.5578).

2,2-Dimethyl-5-methoxy-5-acetyl-7-hydroxy-2*H*-benzo-[*b*]pyran (19) (method B, preferred procedure for dihydric phenols). To 50 mL (0.1 mol) of 2.0 M diethylmagnesium in diethyl ether was slowly added 18.2 g (0.1 mol) of phloracetophenone monomethyl ether (3-hydroxy-4-acetyl-5-methoxyphenol) in 100 mL of diethyl ether at room temperature, under nitrogen with stirring. The solution was gently refluxed for 30 min, then most of the ether was distilled off and toluene (200 mL) was added. Distillation was continued until the temperature rose to 110 °C in order to remove the ether completely. After cooling at room temperature, a solution of 12.6 g (0.15 mol) of 3-methylbut-2-enal in 200 mL of toluene was added dropwise with stirring and the volume was adjusted to 500 mL with toluene. The mixture was heated with stirring under reflux for 8 h. After cooling, the mass was handled as in method A. Evodionol (19) was obtained from the residue by chromatography on a column of silica gel in hexane–ethyl acetate 9:1; 15.9 g (64%; 95% based on unrecovered starting phenol). A sample obtained by recrystallization from $CHCl_3$–hexane had mp 85–86 °C (lit.[10] mp 86 °C).

Acknowledgment. We are pleased to acknowledge support of this investigation by the Università degli Studi di Parma, Italy.

Registry No.—Titanium(IV) 2-methylphenoxide, 22922-73-2; titanium(IV) 3-methoxyphenoxide, 67859-10-3; titanium(IV) 3,4-dimethoxyphenoxide, 67859-11-4; titanium(IV) sesamoxide, 67859-12-5; titanium(IV) 4-methoxy-1-naphthoxide, 67859-13-6; titanium(IV) 3,5-dimethoxyphenoxide, 67859-14-7; titanium(IV) 3-dimethylaminophenoxide, 67859-15-8; titanium(IV) 3-chlorophenoxide, 67859-16-9; magnesium orcinoxide, 67859-17-0; magnesium olivetoxide, 67859-18-1; magnesium 3-hydroxy-4-acetyl-5-methoxyphenoxide, 67859-19-2.

Supplementary Material Available: Tables III, IV, and V, including analytical and mass spectral data, IR and UV data, and ^1H NMR spectra for new synthesized ecompounds (**5, 6, 7, 9, 11, 13, 14,** and **15**) (3 pages). Ordering information is given on any current masthead page.

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(5) The use of titanium salts of dihydric phenols is not advantageous for synthetic purposes becuase of the low reactivity probably due to aggregation and insolubility in the reaction medium.

(6) The pyridine-catalyzed condensation of 3-methyl-3-hydroxybutyraldehyde dimethyl acetal with olivetol at 170–175 °C affords **17** (7.5%) and **18** (8.3%), yield based on starting olivetol. See ref 3h.

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(8) Melting points (uncorrected) were determined using a Büchi capillary melting point apparatus. IR spectra were determined on a Perkin-Elmer 137 spectrophotometer, UV spectra on a Cary Model 14 recording spectrophotometer, ^1H NMR spectra on a Varian XL-100 instrument, and mass spectra on a Varian CH-5 single focus spectrometer at 70 eV. All chemicals were commercially available or prepared according to standard methods: titanium tetraethoxide and tin tetraethoxide from the corresponding chloride and ethanol in benzene under NH_3; sodium, potassium, litium, and aluminum phenoxides from phenol and Na and K pellets, BuLi, and Al turnings, respectively; magnesium phenoxides from the phenol and $Mg(Et)_2$ in ether; titanium and tin phenoxides by exchange between the phenol and the corresponding ethoxide in toluene under nonequilibrating conditions. Column chromatography was conducted with Merck silica gel 60–230 mesh ASTM. Microanalyses were performed by Istituto di Chimica Farmaceutica dell'Università di Parma, Italy.

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Observations on the Synthesis and Isolation of 2-Methylbenz[*f*]isoindole

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The supposition made by Wittig and Ludwig that 2-methylbenz[*f*]isoindole (**1**) is produced by the action of phenyllithium on 2,2-dimethylbenz[*f*]isoindolinium bromide (**2**) has been shown to be valid. Isolation of **1** from solution was accomplished by treatment of the reaction mixture with *N*-phenylmaleimide, which converted **1** to the stable endo adduct **3**. Support for the structure of **3** was provided by comparison with a specimen prepared from the dienophile and a sample of **1** obtained by the recently reported method of Rettig and Wirz. A new synthesis of **1** by flash vacuum thermolysis of 11-methyl-1,2,3,4-tetrahydroanthracen-1,4-imine (**10**) is described. Compound **10** was prepared by hydrogenation of 11-methyl-1,4-dihydroanthracen-1,4-imine (**9**), obtained by reaction of 1-methylpyrrole with 2,3-didehydronaphthalene (**8**).

Two of the more useful methods for preparing isoindoles are flash vacuum thermolysis (FVT) of nitrogen-bridged six-membered ring systems[1] and the spontaneous decomposition of ylides derived from isoindolinium salts.[2] The latter procedure, discovered by Wittig and co-workers,[2a] is less general in scope since it invariably produces isoindoles with substituents on the nitrogen atom. More recently, Zeeh and König[3] described another route to nitrogen-substituted iso-

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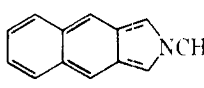

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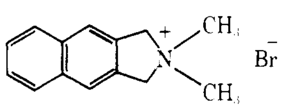

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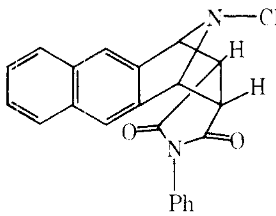
indoles which also employs isoindolinium salts as starting compounds. This method was used by Rettig and Wirz[4] to effect the preparation and isolation of 2-methylbenz[f]isoindole (1). The isolation of compound 1, certainly a milestone in the evolution of the chemistry of isoindoles owing to the compound's extended o-quinoid nature,[5,6] called to mind the earlier failure of Wittig and Ludwig[2b] to isolate 1 from the reaction of phenyllithium with 2,2-dimethylbenz[f]isoindolinium bromide (2). These investigators presented convincing circumstantial evidence that 2-methylbenz[f]isoindole (1) had been formed, but they were unable to isolate 1 from solution nor was it possible to trap the compound as its adduct with maleic anhydride.

Prompted by the work of Rettig and Wirz,[4] we have reexamined the action of phenyllithium on isoindolinium salt 2 and have found that 2-methylbenz[f]isoindole (1) is in fact produced as believed by Wittig and Ludwig. In agreement with their observations, we were unable to isolate 1 or its adduct with maleic anhydride from solution. However, using the more reactive dienophile N-phenylmaleimide, we have succeeded in isolating 1 as the Diels–Alder endo-adduct 3.[7] Since



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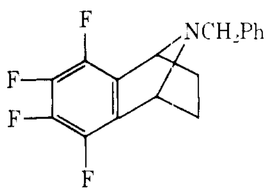
Rettig and Wirz[4] had not described adduct 3 previously, we prepared a sample from 2-methylbenz[f]isoindole obtained by their route; comparison of both specimens of 3 showed them to be identical in all respects.

Earlier, we had reported[1b] that FVT at 600 °C (0.05 mm) of 9-phenylmethyl-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydronaphthalen-1,4-imine (4) affords in quantitative yield 2-phenylmethyl-4,5,6,7-tetrafluorisoindole (5) and ethylene. In



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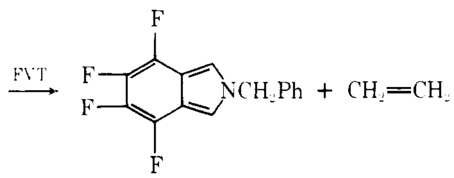

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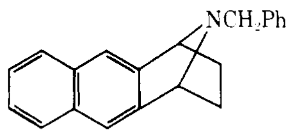
marked contrast and somewhat surprisingly, this technique failed[6] to produce 2-phenylmethylbenz[f]isoindole (7) by retro-Diels–Alder reaction when applied to 11-phenylmethyl-1,2,3,4-tetrahydroanthracen-1,4-imine (6). Examination of 6 by the pyrolysis–GC–MS technique suggested that cleavage of the phenylmethyl group had occurred.[6] The conversion of 4 to 5, on the other hand, clearly indicated that this group can survive the conditions of FVT under certain circumstances. The question, therefore, arose whether this



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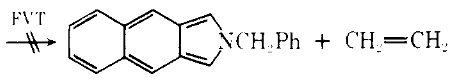

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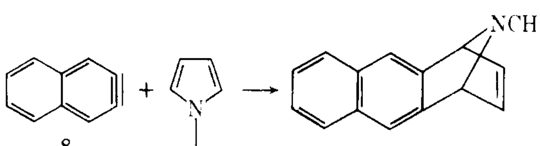
method, which has proven so eminently successful for the preparation of a variety of isoindoles,[8] including the parent[1a] and benz[f]isoindole,[6] was adaptable to the synthesis of nitrogen-substituted benzannellated members of this class of compounds. Consequently, we decided to evaluate FVT as a route to such compounds by attempting the synthesis of 1-methylbenz[f]isoindole (1), an authentic sample[4] of which was already in hand. For this purpose, 11-methyl-1,4-dihydroanthracen-1,4-imine (9) and 11-methyl-1,2,3,4-tetrahydroanthracen-1,4-imine (10), the immediate precursor to 1, were required. Heterocycles 9 and 10 were of interest in their own right, since they represented additional examples of 1,4-nitrogen-bridged anthracenes, the first of which were prepared only recently.[6]

11-Methyl-1,4-dihydroanthracen-1,4-imine (9) was obtained in purified yield of 12–14% by reaction of 1-methylpyrrole with 2,3-didehydronaphthalene (8).[9] Hydrogenation of 9 in the presence of 5% palladium-charcoal afforded 11-methyl-1,2,3,4-tetrahydroanthracen-1,4-imine (10) in 83–95%



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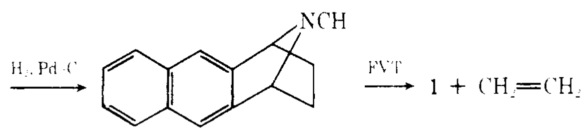

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yield. When 10 was passed through an unpacked quartz tube at 600 °C (0.5 mm), it was converted to 2-methylbenz[f]isoindole 1 and ethylene. Compound 1, which was shown by spectral examination to be identical with the comparison sample prepared by the procedure of Rettig and Wirz,[4] gave a deep purple color with Ehrlich's reagent and decomposed rapidly on exposure to air at room temperature.

The isolation of 2-methylbenz[f]isoindole (1) illustrates further the versatility of the FVT technique. Accordingly, the failure to obtain 2-phenylmethylbenz[f]isoindole (7) from 6 by FVT must be considered a limitation stemming from the compound itself and not the method.

Experimental Section

Melting points were determined on either a Thomas-Hoover or a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Thin-layer chromatography was carried out with Eastman 6060 silica gel and 6063 alumina sheets. Mass spectra were obtained on a Perkin-Elmer Hitachi Model RMS-4 spectrometer. Nuclear magnetic resonance spectra were recorded on a Bruker WH-90 spectrometer or a Perkin-Elmer Hitachi Model R-24 spectrometer; chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane. Ultraviolet–visible absorption spectra were determined with a Cary Model 14 spectrophotometer and infrared spectra were measured with a Perkin-Elmer Model 421 grating spectrometer. Ehrlich's reagent was prepared by mixing 5% ethanolic p-dimethylaminobenzaldehyde with an equal volume of concentrated hydrochloric acid. FVT was carried out in an apparatus similar to those described previously.[1,10]

***N*-Phenylmaleimide Adduct 3 of 2-Methylbenz[*f*]isoindole (1). (a) From 1 Prepared by the Action of Phenyllithium on 2,2-Dimethylbenz[*f*]isoindolinium Bromide (2).** Following the procedure of Wittig and Ludwig,[2b] 5.0 g (18 mmol) of finely powdered **2** was allowed to react with 20 mmol of ethereal phenyllithium. Upon completion of reflux, 50 mL of water was added to the reaction mixture and the yellow ethereal layer was separated and without being dried[10] was run into a solution of 1.71 g (10 mmol) of *N*-phenylmaleimide (NPM) in 100 mL of ether. A white precipitate formed immediately. The mixture, after being set aside for 30 min, was filtered to give 2.02 g (31.6%) of a white powder which showed some signs of decomposition and melting at 160–165 °C, with the major portion of the material having mp 225–231 °C dec. Recrystallization from benzene afforded white crystals of adduct **3**: mp 231–232 °C dec. This substance was shown by TLC (silica gel/CH_3CN), IR, NMR, and MS to be identical with endo-adduct **3** prepared below.

(b) From Compound 1 Prepared by the Procedure of Rettig and Wirz.[4] 2-Methylbenz[*f*]isoindole (**1**) was prepared by heating a mixture of 1.0 g (3.6 mmol) of 2-amino-2-methylbenz[*f*]isoindolinium bromide[4] and 7.0 g of powdered sodium hydroxide in a sublimator (150 °C (0.1 mm)) for 3 h. The yellow needles[12] of **1** which collected on the cold finger had mp 122–126 °C dec in a sealed capillary tube under nitrogen (lit.[4] mp >110 °C dec) and gave a violet color immediately with Ehrlich's reagent. The sublimate was scraped under a blanket of nitrogen into a solution of 0.7 g (4.0 mmol) of *N*-phenylmaleimide (NPM) in 25 mL of anhydrous ether. Vigorous shaking effected solution and shortly thereafter a solid deposited. The reaction mixture, after standing overnight in the refrigerator, was filtered by suction to yield 88 mg (6.9%) of endo-adduct **3**, mp 220–228 °C dec. Two recrystallizations from hexane–benzene (1:1) afforded an analytical sample as white crystals; mp 232–233 °C dec (negative test with Ehrlich's reagent even when a benzene solution of **3** was allowed to stand at room temperature for 6 weeks). Boiling of the adduct in 95% ethanol for 5 min apparently failed to induce dissociation as demonstrated by the absence of a coloration when Ehrlich's reagent was added to the hot solution;[13] IR (KBr) 3042, 2994, 2922, 1766, 1704, 1593, 1495, 1449, 1378, 1278, 1180, 1113, 860, 740, 726, 718, and 685 cm^{-1}; NMR (acetone-d_6) δ 7.82 (m, 2 H, aromatic), 7.67 (s, 2 H, aromatic), 7.42 (m, 2 H, aromatic), 6.91 (m, 3 H, aromatic), 5.97 (m, 2 H, aromatic), 4.66 (m, 2 H, bridgehead), 3.91 (m, 2 H, α to carbonyl), and 2.18 (s, 3 H, CH_3); MS *m/e* 354 (M^+), 181 (M − NPM, retro-Diels–Alder fragment, base peak).

Anal. Calcd for $C_{23}H_{18}N_2O_2$: C, 77.95; H, 5.12; N, 7.91. Found: C, 77.97; H, 5.06; N, 7.93.

11-Methyl-1,4-dihydroanthracen-1,4-imine (9). This reaction was carried out in an atmosphere of dry nitrogen. A stirred slurry of 1.0 g (5.0 mmol) of 2-naphthalenediazonium-3-carboxylate[9] **(Caution: Explosive!)** in 15 mL of purified *p*-dioxane was added in small portions over the course of 30 min to a stirred, refluxing solution of 3.6 g (44 mmol) of 1-methylpyrrole in 45 mL of *p*-dioxane. Immediately upon completion of the addition the source of heat was removed and the reaction mixture allowed to cool slowly to room temperature. Concentration on a rotary evaporator gave a dark brown oil which was dissolved in a minimal amount of dichloromethane and chromatographed on a column containing 75 g of basic alumina (80–200 mesh, Activity I). Elution was performed successively with benzene, benzene–dichloromethane (1:1), and finally dichloromethane. Removal under reduced pressure of the solvent from the dichloromethane fractions afforded a light tan solid (160–180 mg), which was purified by sublimation (50 °C (0.15 mm)) to yield 120–135 mg (12–13%) of **9** as needles: mp 94.5–95.5 °C; UV λ_{max} (heptane) 233, 260, 268, 277, 297, 310, and 325 nm; NMR ($CDCl_3$) δ 7.45 (m, 6 H, aromatic), 6.74 (s, 2 H, olefinic), 4.50 (s, 2 H, bridgehead), and 2.10 (s, 3 H, CH_3); MS *m/e* (rel intensity) 208 (M^+ + 1, 16.52), 207 (M^+, 69.56), 181 (86.95), 166 (86.95), 165 (100).

Anal. Calcd for $C_{15}H_{13}N$: C, 86.92; H, 6.32; N, 6.76. Found: C, 86.65; H, 6.20; N, 6.58.

11-Methyl-1,2,3,4-tetrahydroanthracen-1,4-imine (10). A solution of 100 mg (0.48 mmol) of **9** in 45 mL of 95% ethanol to which 10 mg of 5% palladium–charcoal had been added was shaken with hydrogen at 50 psi for 3 h at room temperature. The reaction mixture was then filtered to remove the catalyst and the filtrate concentrated under reduced pressure to give a nearly white solid. Sublimation at 40 °C (0.15 mm) afforded fluffy white crystals of **10** (84–96 mg, 83–95%), mp 99.5–100.5 °C. Recrystallization of **10** from pentane yielded white needles (88% recovery): mp unchanged; UV λ_{max} (heptane) 224, 263, 273, 284, 306, and 319 nm; NMR ($CDCl_3$) δ 7.48 (m, 6 H, aromatic), 4.08 (s, 2 H, bridgehead), 2.11 (m, 2 H, 2,3-*exo*-hydrogens), 1.99 (s, 3 H, CH_3), and 1.24 (m, 2 H, 2,3-*endo*-hydrogens); MS *m/e* (rel intensity) 209 (M^+, 4.08), 181 (100).

Anal. Calcd for $C_{15}H_{15}N$: C, 86.08; H, 7.22; N, 6.69. Found: C, 86.12; H, 7.27; N, 6.54.

2-Methylbenz[*f*]isoindole (1). Purified **10** (85 mg, 0.41 mmol) was subjected to FVT[1,10] in a vertically aligned unpacked quartz tube (1.6 × 40.0 cm) at 600 °C (0.5 mm). Compound **1** deposited as yellow needles on the cold finger of the trap which was cooled in liquid nitrogen. Replacement of the liquid nitrogen coolant with dry ice caused the coproduct, ethylene, to vaporize leaving **1** in essentially quantitative yield. Compound **1** gave a deep purple color with Ehrlich's reagent and decomposed rapidly in air at room temperature. The purity and identity of **1** were unequivocally established by comparison of its UV–visible and NMR spectra with those of a sample of **1** prepared by the procedure of Rettig and Wirz.[4]

Acknowledgments. We are grateful to Professor George Vogel of the Department for the mass spectra and to Professor Alfred G. Redfield of Brandeis University for making available to us the Bruker WH-90 NMR spectrometer. National Science Foundation Grants GP-37156 and GU-3852 made purchase of this instrument possible.

Registry No.—**1**, 59788-14-6; **2**, 24000-32-6; **3**, 68438-19-7; **9**, 68438-20-0; **10**, 68438-21-1; 2-amino-2-methylbenz[*f*]isoindolinium bromide, 68438-22-2; 2-naphthalenediazonium-3-carboxylate, 30013-85-5; *N*-phenylmaleimide, 941-69-5; 1-methylpyrrole, 96-54-8; phenyllithium, 591-51-5.

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(6) Benz[*f*]isoindole has been isolated recently by D. E. Remy, F. H. Bissett, and J. Bornstein, *J. Org. Chem.*, **43**, 4469 (1978).
(7) The endo assignment of **3** is based on the multiplicity of the NMR spectrum at δ 4.66 and 3.91 consistent with coupling of the bridgehead protons and their vicinal neighbors. See: M. Karplus, *J. Am. Chem. Soc.*, **85**, 2870 (1963), and M. Cava, N. Pollack, O. Mainer, and M. Mitchell, *J. Org. Chem.*, **36**, 3932 (1971).
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(11) Drying the ethereal solution considerably decreases the yield of adduct **3**.
(12) Rettig and Wirz (ref 4) ascribed an orange color to 2-methylbenz[*f*]isoindole (**1**). We observed this color only after **1** had been heated at higher temperature under vacuum for an extended period of time.
(13) Diels–Alder adducts of some isoindoles undergo dissociation in solution. See: J. E. Shields and J. Bornstein, *J. Am. Chem. Soc.*, **91**, 5192 (1969), and references cited therein.