N-Trimethylsilylpyrroles as Dienes in the Synthesis of 1,4-Dihydronaphthalen-1,4-imines and Isoindoles (1)

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A convenient, general synthetic method for 1,4-dihydronaphthalen-1,4-imines *via* the Diels-Alder addition of benzyne to *N*-trimethylsilylpyrrole is described. The *N*-trimethylsilyl protecting group protected the product from secondary benzyne reactions and was easily removed. The use of a 1,3-dipolar reagent to convert 1,4-dihydronaphthalen-1,4-imines to isoindoles *via* a retro-Diels-Alder sequence is illustrated.

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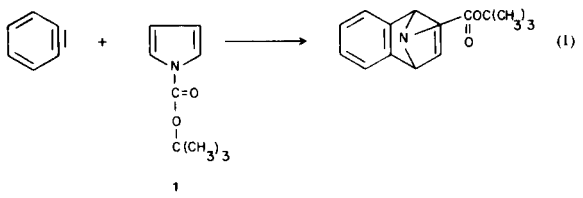
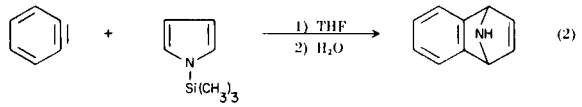
The Diels-Alder addition of acetylenes to isoindoles or alternatively the cycloaddition of benzynes to pyrroles are the only suitable synthetic methods for the construction of 1,4-dihydronaphthalen-1,4-imines. These approaches have limitations and drawbacks which have been described adequately elsewhere (2). In general, the cycloaddition of benzyne to *N*-*t*-butoxycarbonylpyrrole (**1**) as shown in Eq. 1 is the most useful and consequently most frequently applied variation of this method (3). Although the *N*-protecting group minimizes secondary benzyne reactions, its removal to obtain the desired imine product requires an additional carefully controlled cleavage step under acidic conditions.



(1)

1

Difficulties encountered in the removal of this protecting group from certain acid sensitive naphthalenimines as well as the failure of tetrafluorobenzyne to add smoothly to **1** prompted a search for an alternative way to circumvent these problems. Described below and shown in Eq. 2 is a new procedure which largely overcomes the limitations of previous methods and, thus, significantly enhances the overall synthetic utility of the Diels-Alder approach to 1,4-dihydronaphthalen-1,4-imines.



(2)

In the cycloaddition method set forth here, an *N*-trimethylsilylpyrrole is used as the diene (4). The choice of the *N*-protecting group was based on the ease of synthesis of the necessary *N*-trimethylsilylpyrroles (5), the expected ability of this group to protect both the pyrrole and the product from secondary benzyne reactions, and its facile removal from the product. The meeting of these criteria and the general utility of this application of *N*-trimethylsilylpyrroles as dienes in cycloaddition reactions with benzynes are illustrated in Table I. The reaction was successful with unsubstituted 2,5-disubstituted and 3,4-disubstituted-*N*-trimethylsilylpyrroles undergoing cycloaddition with benzynes having a broad range of chemical reactivity. In practice, the yield of naphthalenimine was somewhat sensitive to the method used to generate the benzyne. Thus, benzynes containing a methoxy or methyl substituent gave the best results when generated from an *o*-dihalobenzene and magnesium metal in THF containing the *N*-trimethylsilylpyrrole (method B). The method of choice for halo-, tetrahalo- and trifluoromethylbenzyne was to treat a mixture of the appropriate benzyne precursor with *n*-butyllithium at -60° in ether followed by addition of the *N*-trimethylsilylpyrrole (method A) (6).

A most important advantage of this approach, however, is the removal of the *N*-protecting group under mild conditions (addition of water) rather than the strongly acidic conditions required by published procedures. Thus, even extremely acid sensitive 1,4-dihydronaphthalen-1,4-imines can be prepared using this technique. It also should be noted that excess *N*-trimethylsilylpyrrole used in the reaction is not hydrolyzed by water and may be recovered by distilliation. The yields of imines obtained in this one-step procedure are comparable to those obtained in the two-step Carpino scheme. As an illustration, 6-fluoro-1,4-dihydronaphthalen-1,4-imine (**14**) was prepared by both methods, the yield being 49% using *N*-trimethylsilylpyrrole (**3**) and 41% with *N*-*t*-butoxycarbonylpyrrole (**1**).

Many of the 1,4-dihydronaphthalenimines described here were sensitive to mineral acids and prolonged exposure to light and air; however, they were conveniently stored as stable, crystalline fumaric acid salts. These salts served a second useful purpose in that addition of aldehydes and sodium cyanoborohydride to an acetonitrile solution of the salt effected a Borch (7) type reductive alkylation as described for **10** in the experimental section. Furthermore, the imine was obtainable without decomposition on neutralization of aqueous solutions of these salts.

The structures of the naphthalenimines were determined by their characteristic proton nmr and mass spectra. The 1,2,3,4-unsubstituted 1,4-dihydronaphthalen-1,4-imines exhibited degenerate A_2X_2 signals (2) for the bridgehead and olefinic protons which appeared as triplets near 5.5 and 7.1 δ, respectively. These signals were reduced to singlets by spin decoupling. In the case of the tetrafluoro analogs **4** and **23**, the bridgehead protons were also weakly coupled to the aromatic fluorines at C-5 and C-8. The mass spectra of these compounds exhibited a molecular ion of moderate intensity and a fragmentation pattern dominated by a retro-Diels-Alder reaction to the appropriate isoindole and its subsequent degradation. The most intense ion in each spectrum was that of the isoindole.

A number of recent publications have indicated the utility of the retro-Diels-Alder reaction of naphthaleneimines for the synthesis of isoindoles (8,9). Because previously unreported 5,6,7,8-tetrafluoro-1,4-dihydronaphthalen-1,4-imine (**4**) became readily available by the procedure described here, its retro-Diels-Alder conversion to 4,5,6,7-tetrafluoroisoindole (**29**) was of interest as a synthetic method. Thus the approach described below was designed to take advantage of the dipolarophilic reactivity of an angle-strained double bond. The choice of an appropriate 1,3-dipolar reagent which would convert **4** to an adduct having a low activation energy toward subsequent retro-cycloaddition would provide a facile pathway to isoindole. Nitrilimines and nitriloxides appeared to be attractive candidates for effecting this conversion, since the retro-cycloaddition would lead to pyrazoles and isoxazoles, respectively (10).

Treatment of a benzene solution of **23** with the nitriloxide precursors, benzhydroxamic acid chloride (**24**) or acetyl hydroxamic acid chloride (**25**), and triethylamine gave only the relatively stable *exo* 1,3-dipolar adducts **26** and **27**. However, addition of triethylamine to a benzene solution of the diphenylnitrilimine precursor *N'*-α-chlorobenzylidene-N^2-phenylhydrazine (**28**) and the naphthalenimine **23** at room temperature afforded 2-methyl-4,5,6,7-tetrafluoroisoindole (**30**) and 1,3-diphenylpyrazole (**31**) in nearly quantitative yield a few minutes after mixing. Repeating this procedure with **4** gave the isoindole **29** which was purified by fractional sublimation and then characterized by nmr and mass spectral properties. Treatment of **29** with *N*-phenylmaleimide effected conversion to a mixture of the *endo* and *exo* adducts **32** and **33** which were separated by column chromatography on silica gel. The adducts **32** and **33** were readily distinguishable by proton nmr because the *exo* hydrogens in **32** have a larger coupling to the bridgehead protons than is the case with **33**.

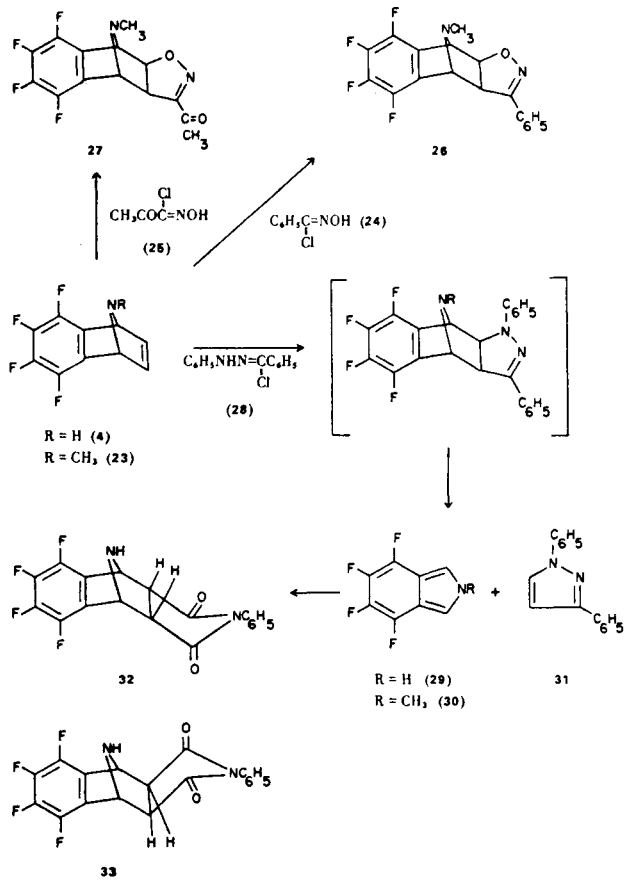
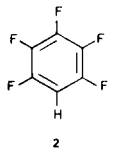
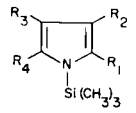
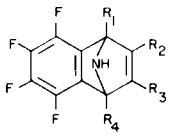
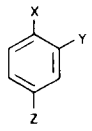
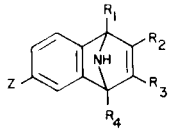
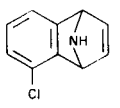


Table I

Compound No.	Reactants		Product (a)	Method	Yield (b)
	 2	+ 			
I	2(c)	$R_1 = R_2 = R_3 = R_4 = H$ (3)(d)	$R_1 = R_2 = R_3 = R_4 = H$ (4)	A	35
II	2	$R_1 = R_4 = H$, $R_2 = R_3 = CH_3$ (5)	$R_1 = R_4 = H$, $R_2 = R_3 = CH_3$ (6)	A	38
					
III	X = Br, Y = I Z = OCH_3 (7)(e)	3	$R_1 = R_2 = R_3 = R_4 = H$ Z = OCH_3 (8)	B	39
IV	X = Cl, Y = Br Z = CF_3 (9)(f)	3	$R_1 = R_2 = R_3 = R_4 = H$ Z = CF_3 (10)	A	39
V	X = Cl, Y = Br Z = CH_3 (11)(g)	3	$R_1 = R_2 = R_3 = R_4 = H$ Z = CH_3 (12)	B	41
VI	X = Z = F, Y = Br (13)(h)	3	$R_1 = R_2 = R_3 = R_4 = H$ Z = F (14)	A	49
VII	13	5	$R_1 = R_4 = H$, $R_2 = R_3 = CH_3$ Z = F (15)	A	53
VIII	13	$R_1 = R_4 = H$, $R_2 = R_3 = Cl$ (16)	$R_1 = R_4 = H$, $R_2 = R_3 = Cl$ Z = F (17)	A	40
IX	X = Br, Y = F Z = H, (18)(i)	$R_1 = R_4 = CH_3$, $R_2 = R_3 = H$ (19)	$R_1 = R_4 = CH_3$, $R_2 = R_3 = H$ Z = H (20)	B	30
X	2,6-dichlorobromo-benzene (21)(j)	3	 22	B	34

(a) All compounds exhibited H^1 nmr spectra consistent with the assigned structure. (b) Yields are reported for crystalline fumaric acid salts having satisfactory analyses (± 0.4% C, H, and N). (c) PCR, Inc., commercial sample. (d) Prepared as described in reference 5. (e) Prepared as described in reference 11. (f) Chemical Procurement Labs., Inc., commercial sample. (g) Prepared as described in reference 12. (h) Pierce Chemical Company, commercial sample. (i) Aldrich Chemical Company, commercial sample. (j) Compound **21** has been described previously (19) and was prepared here by diazotization of 2,6-dichloroaniline.

In summary a new preparative method for 1,4-dihydronaphthalen-1,4-imines has been developed and a new reagent for the conversion of these imines to isoindoles has been described.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover "Unimelt" capillary melting point apparatus and are uncorrected. Boiling points are uncorrected. Nmr spectra were recorded on a Varian T-60A spectrometer using tetramethylsilane as an internal standard for proton spectra and fluorotrichloromethane for ^{19}F spectra. Infrared spectra were recorded on a Perkin Elmer 257 grating spectrophotometer. Glc data were obtained on a Hewlett-Packard Model 5700A/3370B GLC using a glass column (6' by 2 mm) packed with 1% OV-17 on 100/120 Gas-Chrom Q.

N-Trimethylsilyl-2,5-dimethylpyrrole (**19**).

A solution of 2,5-dimethylpyrrole (28.5 g., 0.3 mole) in ether (100 ml.) and benzene (40 ml.) was stirred in a nitrogen atmosphere and treated with small pieces of potassium (11 g.) added portionwise. After heating under reflux for 6 hours, chlorotrimethylsilane (30 g.) was added dropwise over 30 minutes and

stirring was continued overnight. The reaction mixture was filtered and distilled to yield 36 g. (72%) of **19**, b.p. 95-97° (15 mm.) [lit. (18) b.p. 91-93° (18 mm.)] glc purity >96%; H^1 nmr (deuteriochloroform): δ 0.5 (s, 9H, $Si(CH_3)_3$), 2.38 (s, 6H, CH_3), 5.9 (s, 2H, =C-H); ir (neat): 1520, 1120, 1015, 845, 765 cm^{-1}. This reagent was used without further purification.

N-Trimethylsilyl-3,4-dichloropyrrole (**16**).

A mixture of 3,4-dichloropyrrole (16) (6.8 g., 0.05 mole), ammonium sulfate (20 mg.) and 1,1,1,3,3,3-hexamethyldisilazane (17.5 ml.) was heated at 110-120° for 12 hours. Distillation of the reaction mixture gave **16** (10.4 g., 100%), b.p. 97° (0.2 mm.); H^1 nmr (deuteriochloroform): δ 0.46 (s, 9H, $-Si(CH_3)_3$), 6.69 (s, 2H, C-H); ir (neat): 1510, 1260, 1080, 970, 850 cm^{-1}; GLC purity > 97%. This reagent was used without further purification.

N-Trimethylsilyl-3,4-dimethylpyrrole (**5**).

A mixture of 3,4-dimethylpyrrole (17) (12 g., 0.13 mole) ammonium sulfate (20 mg.) and 1,1,1,3,3,3-hexamethyldisilazane (23 g., 0.14 mole) was heated at 125° for 12 hours. Distillation of the reaction mixture gave **5** (20 g., 95%), b.p. 83-85° (17 mm.); H^1 nmr (deuteriochloroform): δ 0.36 (s, 9H, $-Si(CH_3)_3$), 2.01 (s, 6H, CH_3-), 6.49 (s, 2H, NCH=); GLC purity > 96%. This reagent was used without further purification.

6-Trifluoromethyl-1,4-dihydronaphthalen-1,4-imine Fumarate (**10**). Method A.

A flame dried flask was flushed with nitrogen and cooled to -70°. This reaction vessel was charged with ether (20 ml.), *n*-butyllithium in hexane (6 ml., 1.8 molar) and then an ether (10 ml.) solution of **9** (2.6 g., 0.01 mole). A solution of **3** (3 ml.) in ether (10 ml.) was added with stirring and the reaction mixture was allowed to warm slowly to room temperature over 2 hours. Water was added and the aqueous layer was extracted with ether (3 x 100 ml.). The combined organic extracts were dried over anhydrous sodium sulfate, the drying agent separated by filtration and the filtrate evaporated to an oil. This residue was dissolved in warm 2-propanol (50 ml.). Cooling gave 1.5 g. (39%) of **10**, m.p. 162-163°; H^1 nmr (deuteriochloroform): δ 5.60 (t, 2H, bridgehead H), 6.59 (s, 3H, olefinic H of acid), 7.17 (t, 2H, olefinic H), 7.60 (m, 3H, aromatic), 11.40 (s, 4H, CO_2H, NH, exchanged by deuterium oxide).

Anal. Calcd. for $C_{11}H_8F_3N \cdot 1.5C_4H_4O_4$: C, 52.99; H, 3.66; N, 3.64. Found: C, 53.29; H, 3.81; N, 3.59.

5,6,7,8-Tetrafluoro-1,4-dihydronaphthalen-1,4-imine Fumarate (**4**).

Method A was used to prepare from **2** (7.5 g., 0.044 mole), *n*-butyllithium in hexane (30 ml., 1.9 molar) and **3** (10 ml.) a 5.9 g. (35%) yield of **4**, m.p. 201-203°; H^1 nmr (DMSO-d_6): δ 5.5 (m, 2H, bridgehead H), 6.8 (s, 3H, olefinic H of fumaric acid), 7.16 (m, 2H, olefinic H), 10.7 (s, 3H, CO_2H + NH, exchanged by deuterium oxide); ^{19}F nmr (deuteriochloroform + sodium deuteroxide): δ 142 (m, 2F, aromatic at C-5 and C-8), 157 (m, 2F, aromatic at C-6 and C-1).

Anal. Calcd. for $C_{10}H_5F_4N \cdot 1.5C_4H_4O_4$: C, 49.50; H, 2.82; N, 3.60. Found: C, 49.59; H, 2.97; N, 3.54.

2,3-Dimethyl-5,6,7,8-tetrafluoro-1,4-dihydronaphthalen-1,4-imine Hydrogenfumarate (**6**).

Method A was used to prepare from *n*-butyllithium in hexane (22 ml., 1.9 molar), **2** (6.2 g., 0.037 mole) and **5** (7.2 g., 0.04 mole) a 5.0 g. (38%) yield of **6**, m.p. 184-185°; H^1 nmr (DMSO-d_6): δ 1.72 (s, 6H, CH_3), 5.17 (s, 2H, bridgehead), 6.48 (s, 2H, olefinic H of fumaric acid), 10.3 (s, 3H, CO_2H and NH).

Anal. Calcd. for $C_{12}H_9F_4N \cdot C_4H_4O_4$: C, 53.45; H, 3.64; N, 3.89. Found: C, 53.60; H, 3.77; N, 3.72.

2,3-Dimethyl-6-fluoro-1,4-dihydronaphthalen-1,4-imine Fumarate (**15**).

Method A was used to prepare from **13** (5.7 g., 0.03 mole), **5** (5.5 g., 0.033 mole) and *n*-butyllithium in hexane (17 ml., 1.9 molar), a 5.7 g. (53%) yield of **15**, m.p. 204-205°; H^1 nmr (DMSO-d_6): δ 1,7 (s, 6H, CH_3-), 5.31 (s, 2H, bridgehead H), 6.55 (s, 3H, olefinic H of fumaric acid), 6.8-7.6 (m, 3H, aromatic), 11.6 (s, 4H, CO_2H and NH, exchanged by deuterium oxide).

Anal. Calcd. for $C_{12}H_{12}FN \cdot 1.5C_4H_4O_4$: C, 59.40; H, 4.99; N, 3.84. Found: C, 59.10; H, 5.29; N, 3.65.

2,3-Dichloro-6-fluoro-1,4-dihydronaphthalen-1,4-imine Fumarate (**17**).

Method A was used to prepare from **13** (3.8 g., 0.02 mole), **16** (3.9 g., 0.02 mole) and *n*-butyllithium in hexane (20 ml., 1.9 molar), a (36%) yield of **17**, m.p. 202-203°; H^1 nmr (DMSO-d_6): δ 4.96 (s, 2H, bridgehead H), 6.65 (s, 3H, olefinic H of fumaric acid), 7.1 (m, 3H, aromatic), 10.5 (s, 4H, CO_2H and NH, exchanged by deuterium oxide).

Anal. Calcd. for $C_{10}H_6Cl_2FN \cdot 1.5C_4H_4O_4$: C, 47.54; H, 2.99; N, 3.47. Found: C, 47.52; H, 2.98; N, 3.32.

6-Fluoro-1,4-dihydronaphthalen-1,4-imine Hydrogenfumarate (**14**).

Method A was used to prepare from **13** (20 g., 0.103 mole), *n*-butyllithium in hexane (55 ml., 1.9 molar) and **3** (21 g., 0.15 mole), a 13.7 g. (49%) yield of **14**, m.p. 160-161°; H^1 nmr (DMSO): δ 5.50 (t, 2H, bridgehead H), 6.60 (s, 2H, olefinic of fumaric acid), 7.15 (t, 2H, olefinic H), 9.33 (s, 3H, CO_2H and NH), 6.8-7.6 (m, 3H, aromatic).

Anal. Calcd. for $C_{10}H_8NF \cdot C_4H_4O_4$: C, 60.64; H, 4.34; N, 5.06. Found: C, 60.70; H, 4.57; N, 4.86.

Method B. 6-Methoxy-1,4-dihydronaphthalen-1,4-imine Hydrogenfumarate (**8**).

A solution of **7** (12.6 g., 0.04 mole) in THF (50 ml.) was added dropwise to a stirred slurry of magnesium metal (1.0 g., 0.04 mole) and **3** (8.3 g., 0.06 mole) in refluxing THF (50 ml.) under a nitrogen atmosphere. The reaction mixture was heated under reflux for 3 hours, cooled and poured into ice water. The aqueous mixture was extracted with ether (3 x 100 ml.), the combined extracts dried over sodium sulfate, the drying agent separated by filtration and the filtrate concentrated *in vacuo*. Distillation of the residue gave 2.9 g. of product, b.p. 80-88° (0.5 mm.), which was dissolved in ethyl acetate (20 ml.) and added to fumaric acid (2.3 g.) in warm 2-propanol (60 ml.). Cooling gave 4.3 g. (39%) of **8**, m.p. 170-172°; H^1 nmr (DMSO-d_6): δ 3.8 (s, 3H, OCH_3), 5.45 (t, 2H, bridgehead), 6.57 (s, 2H, olefinic H of fumaric acid), 6.65 (dd, 1H, J = 8 Hz, J = 2 Hz, aromatic), 7.17 (t, 2H, olefinic H), 7.2 (d, 1H, J = 2 Hz, aromatic), 7.42 (d, 1H, J = 8 Hz, aromatic), 8.66 (s, 3H, $-CO_2H$ and N-H, exchanged by deuterium oxide).

Anal. Calcd. for $C_{12}H_{13}NO \cdot C_4H_4O_4$: C, 63.36; H, 5.60; N, 4.61. Found: C, 63.41; H, 5.90; N, 4.48.

6-Methyl-1,4-dihydronaphthalen-1,4-imine Hydrogenfumarate (**12**).

This compound was prepared by Method B from **3** (12 ml.), magnesium metal (1.2 g., 0.05 mole) and **11** (10.3 g., 0.05 mole) heated under reflux in THF (30 ml.) for 12 hours. The crude product was distilled and the fraction b.p. 85-100° (0.2 mm.) dissolved in ethyl acetate and added to fumaric acid in warm 2-propanol to yield 5.2 g. (41%) of **12**, m.p. 171-173°; H^1 nmr

(DMSO-d_6); δ 2.27 (s, 3H, CH_3-), 5.45 (t, 2H, bridgehead H), 6.49 (s, 2H, olefinic H of fumaric acid), 7.1 (m, 5H, olefinic and aromatic), 11.4 (s, 3H, CO_2H and NH, exchanged by deuterium oxide).

Anal. Calcd. for $C_{11}H_{11}N \cdot C_4H_4O_4$: C, 65.92; H, 5.53; N, 5.12. Found: C, 65.77; H, 5.57; N, 4.91.

1,4-Dimethyl-1,4-dihydronaphthalen-1,4-imine Hydrogenfumarate (**20**).

Method B was used to prepare from **18** (5.25 g., 0.03 mole), magnesium metal (0.72 g., 0.03 mole) and **19** (9.0 g., 0.054 mole) a 2.6 g. (30%) yield of **20**, m.p. 166-167°; H^1 nmr (DMSO-d_6): δ 1.85 (s, 6H, CH_3), 6.41 (s, 2H, olefinic H of fumaric acid), 6.83 (s, 2H, olefinic), 7.17 (m, 4H, aromatic), 10.8 (s, 3H, CO_2H and N-H, exchanged by deuterium oxide).

Anal. Calcd. for $C_{12}H_{13}N \cdot C_4H_4O_4$: C, 66.88; H, 5.96; N, 4.86. Found: C, 66.51; H, 6.10; N, 4.74.

5-Chloro-1,4-dihydronaphthalen-1,4-imine Hydrogenfumarate (**22**).

Method B was used to prepare from **21** (5.6 g., 0.025 mole), magnesium metal (0.6 g., 0.025 mole) and **3** (8 ml.) a 2.5 g. (34%) yield of **22**, m.p. 157°; H^1 nmr (DMSO-d_6): δ 5.41 (t, 2H, bridgehead), 6.59 (s, 2H, olefinic H of fumaric acid), 7.2 (t, 2H, olefinic H), 7.0-7.5 (m, 3H, aromatic), 9.5 (s, 3H, CO_2H and NH, exchanged by deuterium oxide).

Anal. Calcd. for $C_{10}H_8ClN \cdot C_4H_4O_4$: C, 57.75; H, 4.12; N, 4.74. Found: C, 57.62; H, 4.25; N, 4.71.

Reaction of 9-Methyl-5,6,7,8-tetrafluoro-1,4-dihydronpahthalen-1,4-imine (**23**) with Acetylhydroxamic Acid Chloride (**25**) (14).

A solution of **23** (4.6 g., 0.02 mole) and **25** (2.44 g., 0.02 mole) in benzene (100 ml.) was treated dropwise with triethylamine (3 g.). After stirring overnight, the reaction mixture was washed with 5% aqueous sodium hydroxide solution (50 ml.) and water (50 ml.). The organic solution was dried over sodium sulfate, filtered and evaporated. The resulting oily residue was chromatographed on silica gel. Elution with chloroform gave **23** (0.6 g.) followed by 2.3 g. (36%) of the 1,3-dipolar adduct **27**, m.p. 132-134° (acetone-hexane); H^1 nmr (deuteriochloroform): δ 2.13 (s, 3H, N-CH_3), 2.53 (s, 3H, CH_3CO), 3.67 (d, 1H, J = 8 Hz, endo H), 4.76 (m, 2H, bridgehead H), 4.90 (d, 1H, J = 8 Hz, endo H).

Anal. Calcd. for $C_{14}H_{10}F_4N_2O_2$: C, 53.50; H, 3.20; N, 8.91. Found: C, 53.59; H, 3.32; N, 9.04.

Reaction of **23** with *p*-Chlorobenzhydroxamic Acid Chloride (**24**) (13).

A solution of triethylamine (0.5 g.) in benzene (5 ml.) was added dropwise to a stirred solution of **23** (1.15 g., 0.005 mole) and **24** (0.95 g., 0.005 mole) in benzene (50 ml.). After stirring overnight, the reaction mixture was diluted with chloroform (75 ml.) and washed with 5% aqueous sodium hydroxide (50 ml.) and water (50 ml.). The organic solution was dried over sodium sulfate, filtered and evaporated. The residue was recrystallized from hexane to yield 1.1 g. (58%) of the adduct **26**, m.p. 127-129°; H^1 nmr (deuteriochloroform): δ 2.13 (s, 3H, N-CH_3), 3.88 (d, 1H, J = 8 Hz, endo H), 4.58 (m, 1H, bridgehead), 4.75 (m, 1H, bridgehead), 4.88 (d, 1H, J = 8 Hz, endo H), 7.40 (d, 2H, J = 9 Hz, aromatic), 7.60 (d, 2H, J = 9 Hz, aromatic).

Anal. Calcd. for $C_{18}H_{11}ClF_4N_2O$: C, 56.48; H, 2.87; N, 7.32. Found: C, 56.26; H, 3.00; N, 7.18.

Reaction of **23** with *N'*-α-Chlorobenzylidene-N^2-phenylhydrazine (**28**) (15).

Triethylamine (6 g.) was added dropwise to a stirred solution of **23** (4.6 g., 0.02 mole) and **28** (4.6 g., 0.02 mole) in benzene (100 ml.). After stirring for 2 hours, the reaction mixture was washed with 5% aqueous sodium hydroxide (50 ml.) and water (50 ml.). The organic solution was dried over sodium sulfate, filtered and evaporated. Recrystallization of the residue from acetone-hexane gave 3.6 g. (90%) of **30**, m.p. 179-180° (lit. (9) 178°), H^1 nmr (deuteriochloroform): δ 4.02 (s, 3H, NCH_3), 7.21 (m, 2H, =CH-N).

Reaction of 5,6,7,8-Tetrafluoro-1,4-dihydronaphthalen-1,4-imine (**4**) with **28**.

Triethylamine (5 ml.) was added dropwise with stirring to a solution of **4** (3.0 g., 0.014 mole) and **28** (3.4 g., 0.014 mole) in benzene (50 ml.). After 1.5 hours, the reaction mixture was diluted with methylene chloride (150 ml.) and washed with 10% sodium carbonate solution (100 ml.). The organic solution was dried over sodium sulfate, filtered and the filtrate evaporated. Sublimation of the residue at 80° (0.1 mm.) followed by resublimation at 25-40° (0.05 mm.) gave 2.0 g. (77%) of 5,6,7,8-tetrafluoroisoindole (**29**), m.p. 135-137° (lit. (9) 135-136°); ir (Nujol): 3460 cm^{-1}; H^1 nmr (deuteriochloroform): δ 7.4 (m); ^{19}F nmr (deuteriochloroform): δ 150.3 (m, 2F, aromatic at C-5 and C-8), 167 (m, 2F, aromatic at C-6 and C-7); mass spectrum: m/e 189 (M^+), 162 and 143.

Reaction of 4,5,6,7-Tetrafluoroisoindole (**29**) with *N*-Phenylmaleimide.

A solution of *N*-phenylmaleimide (1.0 g., 0.0058 mole) and **29** (0.95 g., 0.005 mole) in ether (25 ml.) was allowed to stand at room temperature in a nitrogen atmosphere for 4 days. Filtration gave 1.6 g. (88%) of a 1:1 mixture of the adducts **32** and **33**. Column chromatography on silica gel (60 mesh) eluted with chloroform effected a clean separation of **32** and **33**. Compound **32** had m.p. 226-228°; H^1 nmr (deuteriochloroform): δ 3.0 (broad singlet, 1H, NH), 3.93 (m, 2H, exo H), 5.3 (m, 2H, bridgehead H), 6.90 and 7.5 (m, 5H, aromatic). Compound **33** had m.p. 224-226°; H^1 nmr (DMSO-d_6): 3.17 (s, 2H, endo H), 4.20 (s, 1H, NH), 5.13 (s, 2H, bridgehead), 7.2-7.65 (m, 5H, aromatic).

Anal. Calcd. for $C_{18}H_{10}F_4N_2O_2$: C, 59.67; H, 2.78; N, 7.73. Found (**32**): C, 59.84; H, 2.89; N, 7.87. Found (**33**): C, 59.91; H, 3.03; N, 7.60.

6-Trifluoromethyl-9-methyl-1,4-dihydronaphthalen-1,4-imine Fumarate (**34**).

A stirred solution of **10** (1.93 g., 0.005 mole) in acetonitrile (40 ml.) was treated with 37% aqueous formaldehyde (2 ml.) and sodium cyanoborohydride (0.50 g.). After stirring for 12 hours, the reaction mixture was treated with 2*N* potassium hydroxide (50 ml.) and extracted with ether (3 x 100 ml.). The combined extracts were dried over sodium sulfate, filtered and the filtrate evaporated. The residue was dissolved in warm 2-propanol containing fumaric acid. On cooling, there was obtained 1.4 g. (70%) of **34**, m.p. 168-170°; H^1 nmr (DMSO-d_6): δ 2.22 (s, 3H, N-CH_3), 5.00 (t, 2H, bridgehead), 6.65 (t, 2H, olefinic), 6.98 (s, 3H, olefinic H of fumaric acid), 7.5 (m, 3H, aromatic), 12.5 (s, 3H, CO_2H, exchanged by deuterium oxide).

Anal. Calcd. for $C_{12}H_{10}F_3N \cdot 1.5\ C_4H_4O_6$: C, 54.25; H, 4.04; N, 3.51. Found: C, 53.94; H, 4.03; N, 3.36.

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