moisture. The cooled reaction mixture was treated with wet ether and filtered, and the filtrate was dried (K_2CO_3) and evaporated to give 1.52 g (90%) of **19** as a colorless oil: bp 68–70° (0.62 mm); ir 3390 cm^{-1}; nmr τ 6.14 (m, 2, CHOH), 7.16 (m, 4, CH_2N), 9.18 (d, 3, J = 7 Hz, CH_3). The crystalline methiodide melted at 263–264° dec.

Anal. Calcd for $C_{11}H_{22}NOI$ (**19** MeI): C, 42.45; H, 7.12; N, 4.49. Found: C, 42.51; H, 7.31; N, 4.43.

General Procedure for Metal–Ammonia Emde Cleavage.—To a 1000-ml three-necked Morton flask equipped with a gas inlet tube, a mechanical stirrer, a cold-finger condenser containing Dry Ice–acetone, and a $CaCl_2$ tube at the exit to the atmosphere was added 300 ml of liquid NH_3, the compound to be reduced, and an equivalent amount of either ethanol (A) or 1-methoxy-2-propanol (B).[15a] The mixture was rapidly stirred as the Li or Na was added in small pieces to give a blue color which sometimes was discharged immediately and sometimes remained until NH_4Cl was added after 10–15 min. Work-up consisted of adding 100 ml of ether, allowing the NH_3 to evaporate, and drying (K_2CO_3) and evaporating the ether. Any ether-insoluble residue in the reaction flask was taken up in hot ethanol to recover unreacted starting material. Reactant and product compositions are listed in Table II. Identification of **6** and **7** was made by comparison with authentic samples and **14**, **20**, and **21** from the analytical and spectral data given below.

5-Phenyl-*N*-methylazacyclononane (**14**) had bp 118–119° (1.8 mm); ir 3060, 3020, 1600, 745, 695 cm^{-1}; nmr τ 2.9 (s, 5, ArH), 7.67 (s, 3, NMe). The crystalline methiodide melted at 187.5–188°.

Anal. Calcd for $C_{16}H_{26}NI$ (**14** MeI): C, 53.49; H, 7.29; N, 3.89. Found: C, 53.55; H, 7.33; N, 3.90.

5-Acetyl-*N*-methylazacyclononane (**20**) had bp 68–69° (0.6 mm); ir 1705 cm^{-1}; nmr τ 7.6 (m, 4, CH_2N), 7.72 (s, 3, NMe), 7.98 (s, 3, CH_3CO). A methiodide was prepared, mp 172.5–173.5°.

Anal. Calcd for $C_{12}H_{24}NOI$ (**20** MeI): C, 44.31; H, 7.44; N, 4.30. Found: C, 44.45; H, 7.61; N, 4.38.

5-(1′-Hydroxyethyl)-*N*-methylazacyclononane (**21**) had bp 79–80° (1.7 mm); ir 3360 cm^{-1}; nmr τ 6.45 (s, 1, OH), 7.67 (m, 4, CH_2N), 7.74 (s, 3, NMe), 8.92 (d, 3, J = 7 Hz, CH_3C). The methiodide had mp 199–200°.

Anal. Calcd for $C_{12}H_{26}NOI$ (**21** MeI): C, 44.05; H, 8.01; N, 4.28. Found: C, 44.17; H, 8.14; N, 4.31.

Reduction of 20.—With the same procedure used to reduce **18** to **19**, 370 mg of **20** was converted to 350 mg (94%) of vpc pure **21** identified by comparison of its ir spectrum with that of a sample prepared as above.

TABLE II
REACTANT AND PRODUCT COMPOSITIONS FOR EMDE CLEAVAGE

Reactant (mmol)	Alcohol	Metal (mmol)	Products (%)
12 MeI (10)	A	Li (20)	**14** (59); **12** MeI (37)
3 MeI (15)	B	Li (30)	**6** (92)
3 MeI (15)	A	Li (30)	**6** (95)
3 MeI (15)	B	Na (30)	**6** (96)
7 (10)	A	Li (20)	**7** (100)
9 MeI (20)	B	Li (40)	**7**, **6**, **17** (6:84:10)[a]
9 MeI (20)	B	Li (60)	**7**, **6**, **17** (12:80:8)[a]
9 MeI (15)	B	Li (15)	**6**, **10**[b]
10 (10)	A	Li (20)	**6**, (91)
18 MeI (10)	A	Li (20)	**20** (68), **21** (28)[c]
18 MeI (10)	A	Na (20)	**20** (78), **21** (17)[c]
20 + **21** (4:1) (10)	A	Li (20)	**21** (94)

[a] In order of increasing retention time; **17** appears to be an artifact formed from probably **11** during vpc treatment at 150°, 200 cm^3/min (see discussion). [b] Spectral analysis of the crude product showed, in addition to absorptions for **6** and **11**, characteristic peaks for **10** at 1950 cm^{-1} in the ir and τ 5.33 (q, J = 2.8 Hz) in the nmr. [c] Separated on a 15 ft × 0.25 in. 15% Carbowax 20M on Chromosorb W column.

Registry No.—**3**, 35201-24-2; **3** MeI, 10478-78-1; **4a**, 35201-26-4; **4a** MeI, 35201-27-5; **4b**, 35201-02-6; **4b** MeI, 35201-03-7; **6**, 35249-63-9; **6** MeI, 35201-04-8; **7**, 35201-05-9; **7** MeI, 35201-06-0; **8** MeI, 35201-07-1; **9**, 35201-08-2; **9** MeI, 35201-09-3; **10**, 35201-10-6; **10** MeI, 35201-11-7; **12**, 35201-12-8; **12** MeI, 35201-13-9; **13**, 35201-14-0; **13** MeI, 35249-64-0; **14**, 35201-15-1; **14** MeI, 35201-16-2; **18**, 35201-17-3; **18** MeI, 35249-65-1; **19**, 35201-18-4; **19** MeI, 35201-19-5; **20**, 35201-20-8; **20** MeI, 35201-21-9; **21**, 35201-22-0; **21** MeI, 35201-23-1.

Acknowledgments.—The authors are grateful for the generous support of this research by the Robert A. Welch Foundation and the T. C. U. Research Foundation.

2H-Cyclopenta[d]pyridazines. Acylation with Trifluoroacetic Anhydride[1,2]

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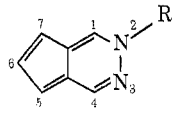
2-Methyl-2*H*-cyclopenta[*d*]pyridazine (**2**) reacts with 1 equiv of trifluoroacetic anhydride in the absence of a catalyst to give the 5- and 7-trifluoroacetyl derivatives (**4**, **5**) in a ratio of *ca.* 1:3. Compounds **4** and **5** react more slowly with the anhydride to form the 5,7-bis(trifluoroacetyl) derivative (**8**). 2-Phenyl-2*H*-cyclopenta[*d*]-pyridazine (**3**) also gives the 5,7-disubstituted compound **10**, but the parent molecule **1** gives only the 7-monosubstituted product **9**. Hydrolysis and esterification of **4** and **5** provide the first route to the corresponding acids (**12**, **14**) and esters (**13**, **15**). Methylation of the anion of **9** occurs only at the 2 position to yield **5**. The nmr and electronic spectra of **4** and **5** are described and discussed.

Subsequent to the demonstration[5] that 2*H*-cyclopenta[*d*]pyridazine (**1**) and its 2-methyl (**2**) and 2-phenyl (**3**) derivatives exhibited spectra and protonation characteristics analogous to those of azulene and simple π-excessive heteroanalogs of azulene, attention



1, R = H
2, R = CH_3
3, R = C_6H_5

(1) Support from the National Science Foundation (GP-5776, GP-9293) is gratefully acknowledged.

(2) From the Ph.D. Theses of David M. Forkey (1967) and Larry D. Grina (1970), University of Washington.

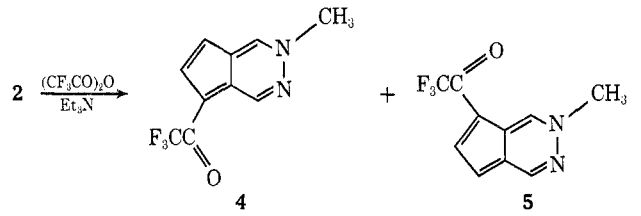
(3) 3M Fellow, 1964–1965; National Science Foundation Summer Fellow, 1965.

(4) National Science Foundation Trainee, 1965–1966; National Defense Education Act Fellow, 1966–1968; National Institutes of Health Fellow, 1968–1970.

(5) A. G. Anderson, Jr., and D. M. Forkey, *J. Amer. Chem. Soc.*, **91**, 924 (1969).

was directed to electrophilic substitution. Trifluoroacetic anhydride was selected as an electrophile, as this reacts rapidly with azulene at room temperature in the absence of a catalyst to give the 1-trifluoroacetyl derivative in high yield.[6] Since the 2*H*-cyclopenta[*d*]pyridazine structure is nonsymmetric, a mixture of the 5- and 7-substitution products was anticipated.

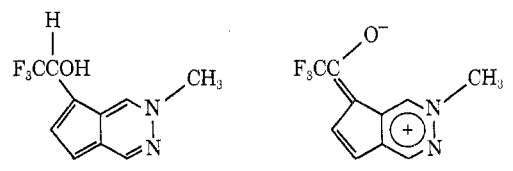
Treatment of **2** with slightly more than 1 equiv of trifluoroacetic anhydride in the presence of 1.5 equiv of triethylamine[7] gave two products, **4** and **5**, in 23



4 5

and 59% yields, respectively. This product ratio corresponds closely to that of the corresponding conjugate acids formed in trifluoroacetic acid.[5] The spectral characteristics of **4** and **5** did not serve to clearly distinguish between them and, accordingly, this was done by X-ray crystallographic analysis of **4** and the 5-bromo derivative of **5**.[8] The peaks in the nmr spectrum of the more soluble isomer, **5**, were assigned as follows: the doublet (J = 1.3 Hz) at δ 9.02 to H-1 (coupling with H-4); the broad singlet at δ 9.58 to H-4 (coupling with H-1 and H-5 not resolved); the doublet (J = 4.2 Hz) at δ 6.77 with subsplitting (J = 1 Hz) to H-5 (coupling with H-6 and H-4, respectively); the singlet (3 H) at δ 4.45 to the *N*-methyl; the multiplet at δ 7.82 to H-6. The limited solubility of **4** required the use of CAT to obtain a spectrum and the couplings between the 1 and 4 and 1 and 7 hydrogens were not resolved. Therefore singlets were observed for H-1 (δ 9.39) and H-4 (δ 9.19), a doublet (J = 4.5 Hz) for H-7 (δ 6.74), a singlet (3 H, δ 4.42) for the *N*-methyl, and, again, a multiplet for H-6 (δ 7.55).

The multiplets for H-6 in these spectra were shown to be due to the H-5(7) and H-6 being part of an ABX_3 system in which H-6 was coupled with the three fluorine atoms of the acetyl group (the fluorine nmr spectrum showed a doublet with J = 2.2 cps). Molecular models showed the most favorable conformation allowing conjugative interaction of the carbonyl with the aromatic ring to be with the trifluoromethyl group directed toward H-6, bringing the hydrogen and fluorines in close proximity and suggesting the possibility of through-space coupling. Reduction of **5** with sodium borohydride afforded the corresponding alcohol **6**. A



6 7

molecular model of **6** showed that the change from a trigonal to a tetrahedral carbon had moved the fluorine atoms away from the 6 hydrogen such that through-space coupling would no longer be possible. In the spectrum of **6** the signals for H-5 and H-6 appeared as a pair of doublets (J = 3.5 Hz) at δ 6.73 and 7.48, respectively.[9] Coupling of H-4 and H-5 (J = 1 Hz) further split the doublet for the former. The peak (couplings of J = 1 Hz with both H-1 and H-5 not resolved) for H-4 was at δ 9.15 and the doublet (J = 1 Hz) for H-1 at δ 8.84. The quartet (J = 8 Hz) for the α hydrogen was at δ 5.57 and the singlet (3 H) for the *N*-methyl at δ 4.19. These data were at first thought to indicate through-space coupling in **4** and **5** for the 6-H–fluorine interaction. The structure of **5** as shown by X-ray analysis,[8] however, indicated that **7** makes an important contribution to the ground state in the solid state, thus effectively extending the π conjugation to the carbon bearing the trifluoromethyl group. Through-bond coupling is therefore also possible.

The visible spectra of **4** and **5** were remarkable in that the long-wavelength absorptions were at 365 and 403 nm, respectively, as compared to 395 nm for **2**. Thus the 7-trifluoroacetyl group caused a bathochromic shift and the 5-trifluoroacetyl group a hypsochromic shift, whereas all acyl groups in the analogous positions on azulene and previously known π-excessive heteroanalogs of azulene had caused hypsochromic shifts. A similar difference in the behavior of **4** and **5** was noted in the effect of solvent polarity on the long-wavelength transition (Table I). As the polarity

TABLE I
EFFECT OF SOLVENT POLARITY ON THE LONG-WAVELENGTH TRANSITION OF 4 AND 5

Compd	Ether (4.34)[a]	Methanol (32.6)	Acetonitrile (37.9)	Formamide (109)
4	365.0	372.0	369.0	378.0
5	403.0[b]	403.0	401.5	404.5

[a] Dielectric constants from N. A. Lange and G. M. Forker, "Handbook of Chemistry," Revised 10th ed, McGraw-Hill, New York, N. Y., 1967, pp 1234–1237. [b] λ_{max}, nm.

was increased, the absorption of **5** changed only slightly, whereas that of **4** exhibited a pronounced bathochromic shift. The carbonyl bands in the infrared spectra indicated about the same degree of interaction of the carbonyl with the aromatic ring for the two isomers, and the nmr absorptions for the *N*-methyl groups (δ 4.42 and 4.45) were very similar.[10] These results were interpreted to indicate that the electronic ground states of the molecules were similar and, therefore, the differences were in the first excited states[11] with an appre-

(6) A. G. Anderson, Jr., and R. G. Anderson, *J. Org. Chem.*, **27**, 3578 (1962).

(7) The amine was added to prevent unreacted **2** from participating as the base to form the conjugate acid, which would not undergo acylation.

(8) H. L. Ammon, P. H. Watts, Jr., A. G. Anderson, Jr., D. M. Forkey, L. D. Grina, and Q. Johnson, *Tetrahedron*, **26**, 5707 (1970).

(9) The spectrum of 1-trifluoroacetyl-4,6,8-trimethylazulene also shows a multiplet for H-2 at δ 2.09, whereas the signal for the corresponding hydrogen in 2-trifluoromethyl-2-hydroxy-5,7-dimethyl-1,2-dihydrocyclopent-[*cd*]azulene is a doublet at δ 2.57 ppm: R. G. Anderson, Ph.D. Thesis, University of Washington, 1961; A. G. Anderson, Jr., R. G. Anderson, and G. T. Hollander, *J. Org. Chem.*, **30**, 131 (1965).

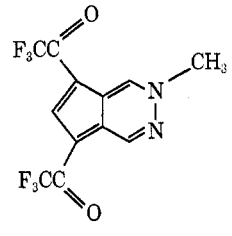
(10) Data on other substitution products have shown the position of the *N*-methyl nmr peak to be sensitive to the electron-withdrawing power of substituents at the 5 and 7 positions: A. G. Anderson, Jr., D. M. Forkey, and L. D. Grina, unpublished results.

(11) It was assumed that the electronic transitions for the two molecules are the same. Alternatively, it is possible that the nonidentity of these transitions is the primary factor involved.

ciable change in the distribution of electronic charge for **4** but little for **5**.[5,12]

The luminescence spectra for **4** and **5** were obtained by Gouterman, Smith, and Seybold.[13a] These spectra showed a factor of 10 difference in the quantum yields of fluorescence for **4** as compared to **5**, while the phosphorescence yields differed by less than a factor of 2 in the opposite direction. Compound **4** lost more than 80% and **5** lost 50% of the absorbed energy by radiationless processes.[13b] Since the lifetimes and quantum yields of phosphorescence were comparable for **4** and **5**, the low quantum yield of fluorescence observed for **4** was not due to increased phosphorescence or a radiationless process from the triplet state, but to a radiationless transition from the singlet to the ground state. This also pointed to a difference in the excited states of **4** and **5**.

Reaction of **2** with an excess of trifluoroacetic anhydride at room temperature gave an 85% yield of the 5,7-bistrifluoroacetyl derivative **8**. The nmr spectrum

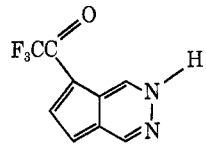


8

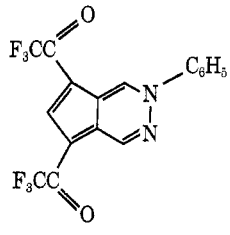
of **8** showed a pair of doublets (J = 1.3 Hz) at δ 9.74 and 10.00 (H-1 coupled with H-4), a multiplet at δ 8.29 (H-6 coupled with the fluorine atoms), and a singlet (3 H) for the N-methyl at δ 4.72.

Since azulene undergoes only monotrifluoroacetylation, even in the presence of Lewis acids,[6] the ease of formation and high yield of **8** was surprising and prompted further experiments. The reaction of **2** with 1 equiv of trifluoroacetic anhydride in the presence of a large excess of triethylamine was carried out to see if **8** might have been formed but not isolated in the earlier run. Only a trace of **8** was found, along with 19% of **4** and 62% of **5**. No unchanged **2** was recovered. Because **2** is relatively unstable, some of it undoubtedly decomposed during the reaction and thus a small excess of anhydride was present. The same reaction except that *ca.* 0.5 equiv of **5** was present in addition to **2** gave 77% of **5** (including unchanged starting material), 18% of **4**, and 9.2% (based on anhydride) of **8**, with no **2** recovered. These results, and those obtained when several separate reactions of **2** with the anhydride were monitored by tlc analysis, indicated that **2** was rapidly converted to **4** and **5** and these products were more slowly converted to **8**. There was no indication of the formation of **8** while **2** was still detectable. Thus the 5- and 7-trifluoroacetyl groups cause some deactivation to further substitution, though much less than in the case of azulene.

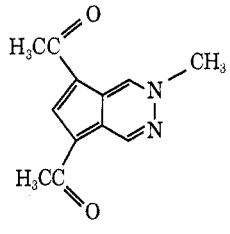
Treatment of **1** with excess trifluoroacetic anhydride and triethylamine for 7 days (the reactions with **2** were complete in 2 days or less), in contrast, gave 49% of the 7-substituted compound **9**, and this reaction with



9



10

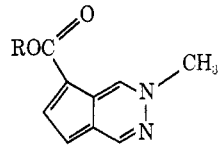


11

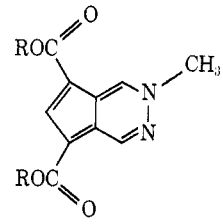
3 (5 days) gave 74% of the 5,7-disubstituted derivative **10** as the only products obtained in significant amounts. The reactivity of the cyclopenta[*d*]pyridazine ring to electrophiles is therefore apparently sensitive to the nature of the substituent on the 1 position with a reactivity order of Me > Ph > H. The methyl group (inductive effect) and the phenyl group (resonance effect) are able to stabilize the transition state relatively more than hydrogen. Compound **9** is indicated to be more stable than the 5-substituted tautomer, and also less reactive to further substitution than **5** and the corresponding derivative of **3**. Further comparative studies on **1**–**3** are planned.

In a single experiment **2** was treated with a large excess of acetic anhydride in the presence of stannic chloride. A 39% yield of the 5,7-diacetyl compound **11** was obtained and the low yield was attributed to side reactions of **2**, **11**, and/or the intermediate monosubstitution products with the stannic chloride.

The hydrolysis of 1-trifluoroacetylazulene in base provides perhaps the best route to 1-azuloic acid and its derivatives.[6] This reaction with **5** provided a product which was judged to be a hydrate of the corresponding carboxylic acid **12**. It was obtained in *ca.* 100%



12, R = H
13, R = CH_3



14, R = H
15, R = CH_3

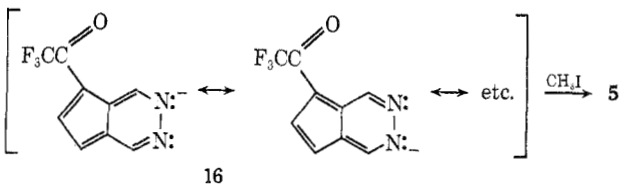
yield and underwent decomposition with decarboxylation[14] on melting or recrystallization. Treatment with diazomethane formed the stable ester **13**. In the same fashion, **14** and **15** were obtained in high yield from **8**. Diacid **14** was also unstable to heat.

The anion of **9** would exist as a resonance hybrid **16** having the potential of undergoing alkylation at

(12) A. G. Anderson, Jr., and B. M. Stecker, *J. Amer. Chem. Soc.*, **81**, 4941 (1959); A. G. Anderson, Jr., W. F. Harrison, and R. G. Anderson, *ibid.*, **85**, 3448 (1963); A. G. Anderson, Jr., and W. F. Harrison, *ibid.*, **86**, 708 (1964).

(13) (a) P. Seybold, Ph.D. Thesis, Harvard University, 1967. (b) Less than 5% of nonradiative energy loss was observed for **8**.

(14) This behavior corresponds to that of 1(3)-azuloic acids.[6]



16

either nitrogen. When **9** was treated with barium oxide and then methyl iodide, however, only one product, **5**, was obtained. A tlc analysis of the reaction mixture did not reveal any trace of the isomeric **4**, and the reaction under the conditions employed was completely selective.

Experimental Section

Melting points were taken on a Fisher or Kofler hot stage and are uncorrected. Ultraviolet and visible spectra were recorded on a Cary Model 14 spectrophotometer. Nmr spectra were recorded on a Varian Model A-60, T-60, or DA-60-11 spectrometer with reference to internal tetramethylsilane. Mass spectra were recorded on an Associated Electrical Industries MS-9 spectrometer. The mass of the parent peak (P) was determined with reference to known peaks of perfluorotributylamine. Hydrocarbon solvents were purified by shaking with sulfuric acid, distillation, and passage through a column of silica gel and basic alumina. Dichloromethane and chloroform were purified by distillation from phosphorus pentoxide and passage through a column of basic alumina. Ether was dried over sodium and distilled. Dimethyl sulfoxide was distilled from the presence of calcium hydride and stored over molecular sieves. Petroleum ether (bp 20–40°) was used and other solvents were reagent grade. Triethylamine was dried over potassium hydroxide pellets. All acylation reactions were monitored by tlc using silica gel G or Merck silica gel GF-254. Unless otherwise specified, organic solutions of products were dried over anhydrous magnesium sulfate.

5- and 7-Trifluoroacetyl-2-methyl-2*H*-cyclopenta[*d*]pyridazine (4 and 5). Method A.—A mixture of 150 mg (1.14 mmol) of **2**, 0.16 ml (1.14 mmol) of trifluoroacetic anhydride, 0.24 ml of triethylamine, and 10 ml of dichloromethane was stirred at room temperature. Unreacted **2** was present (tlc) after 14 hr; so a few drops of the anhydride were added over a period of several hours until analysis for **2** was negative. The mixture was placed in a freezer (−25°) for 16 hr, during which time a solid separated. The precipitate was filtered, washed with H_2O, and air dried to give 58.6 mg (23%) of **4** as a pale, cream-colored solid, mp 233–235°. Three recrystallizations from acetone afforded colorless needles: mp 236–237°; uv max (dry ether) 234 nm (ε 20,200), 244 (18,400), 261 (15,900), 266 (16,100), 293 (18,400), 299 (21,000), and 365 (11,300); nmr (acetone, CAT) δ 9.39 (s, 1), 9.19 (s, 1), 7.55 (m, 1), 6.74 (d, 1, J = 4.5 Hz), and 4.42 ppm (s, 3); ir ($HCCl_3$) 1640 cm^{-1} (C=O); molecular ion at m/e 228.052 (calcd 228.050).

Anal. Calcd for $C_{10}H_7ON_2F_3$: C, 52.63; H, 3.09. Found: C, 52.45; H, 3.11.

Chromatography of the residue from the original filtrate on 200–325 mesh silica gel (dichloromethane eluent) gave 170 mg of **5** as a yellow solid, mp 124.5–130°, which after recrystallization from heptane amounted to 153 mg (59%) of yellow needles, mp 127–129.5°. An additional recrystallization and vacuum drying gave an analytical sample: mp 130.8–131°; uv max (dry ether) 247 nm (ε 23,900), 260 (sh, 15,200), 285 (5720), 295 (5680), 330 (7050), and 403 (9030); nmr (acetone) δ 9.58 (broad s, 1), 9.02 (d, 1, J = 1.3 Hz), 7.82 (m, 1), 6.77 (d of d, 1, J = 4.2 and 1 Hz), and 4.45 ppm (s, 3); ir ($HCCl_3$) 1631 cm^{-1} (C=O).

Anal. Calcd for $C_{10}H_7ON_2F_3$: C, 52.63; H, 3.09. Found: C, 52.99; H, 3.26.

Method B. With 1 Equiv of Trifluoroacetic Anhydride.—The procedure of method A was used with 114.8 mg (0.973 mmol) of **2**, 0.136 ml (0.973 mmol) of trifluoroacetic anhydride, 0.25 ml (1.8 mmol) of triethylamine, and 10 ml of dichloromethane. The mixture was kept at −25° for 24 hr and yielded 39.5 mg (19%) of **4**, mp 234–235°, and 129.4 mg (62.5%) of **5**, mp 121–123°. Recrystallization of the latter from acetone or heptane, sublimation at *ca.* 10^{-3} mm, and drying over P_2O_5 (vacuum) gave material having mp 123–125°. A trace of **8** was identified by tlc (comparison with an authentic sample).

Method C. Trifluoroacetylation of 2 in the Presence of 5.—The procedure of Method B was followed using 103.4 mg (0.885 mmol) of **2**, 71.9 mg (0.336 mmol) of **5**, 0.124 ml (0.885 mmol) of trifluoroacetic anhydride, 0.25 ml (1.8 mmol) of triethylamine, and 10 ml of dichloromethane. The reaction yielded 24.6 mg (18%) of **4**, mp 234–235°, 13.1 mg (9.2%) of **8** as the less polar band from the chromatography, mp 171–172° and, after precipitation from dichloromethane with petroleum ether, 180–181°, and 200.7 mg (77%) of **5**, mp 121–123° (identical with authentic **5** by comparative tlc).

7-(2,2,2-Trifluoro-1-hydroxyethyl)-2-methyl-2*H*-cyclopenta[*d*]-pyridazine (6).[15]—To a magnetically stirred solution of 0.185 g (0.813 mmol) of **5** in 15 ml of methanol was added over *ca.* 10 min a solution of 0.034 g (0.9 mmol) of $NaBH_4$ in 2 ml of methanol. The yellow color of the mixture deepened during the addition. Tlc analysis (silica gel G, dichloromethane, uv light) 25 min after addition showed unchanged **5**, and an additional 3 mg of $NaBH_4$ was added. After 10 min the analysis showed only traces of **5** and the bright yellow solution was chromatographed on a preparative tlc plate (silica gel G, dichloromethane). The material from the separated main yellow band was eluted (dichloromethane) and gave 0.121 g (64.7%) of **6** as a yellow solid, mp 123–133°, molecular ion at m/e 230.0663 (calcd 230.0666). A second tlc procedure afforded yellow crystals from dichloromethane: mp 133–135°; nmr (acetone) δ 9.15 (m, 1), 8.84 (d, 1, J = 1 Hz), 7.48 (d, 1, J = 3.5 Hz), 6.73 (q, 1, J = 3.5 and 1 Hz), 5.57 (q, 1, J = 8 Hz), and 4.19 (s, 3).

Anal. Calcd for $C_{10}H_9ON_2F_3$: C, 52.18; H, 3.94. Found: C, 52.24; H, 3.83.

5,7-Bis(trifluoroacetyl)-2-methyl-2*H*-cyclopenta[*d*]pyridazine (8).—To a cold (ice bath) solution of 110.7 mg (0.841 mmol) of **2** and 0.3 ml of triethylamine in 10 ml of dichloromethane was added 0.35 ml of trifluoroacetic anhydride over a period of 5 min. After another 5 min, the ice bath was removed and the mixture was stirred for 8 hr. An additional 0.1 ml of trifluoroacetic anhydride was added and stirring was continued for 16 hr (tlc analysis showed no **5** to be present and the solution had become red). The solvent was removed (vacuum) and the residue was chromatographed on a 200–325 mesh silica gel column (dichloromethane). Separation of the fluorescent (uv light) portion of the eluate, removal of the solvent (vacuum), and recrystallization of the residue from hexane–dichloromethane gave 231 mg (85%) of **8** as colorless needles: mp 180–180.8°; uv max (dry ether) 252 nm (ε 14,900), 284 (34,800), 302 (17,600), 339 (11,100) and 370 (8300); nmr (acetone) δ 10.0 (d, 1, J = 1.3 Hz), 9.74 (d, 1, J = 1.3 Hz), 8.29 (m, 1), and 4.72 ppm (s, 3); ir ($HCCl_3$) 1653 cm^{-1} (C=O).

Anal. Calcd for $C_{12}H_6O_2N_2F_6$: C, 44.46; H, 1.86; N, 8.64. Found: C, 44.45; H, 1.69; N, 8.63.

7-Trifluoroacetyl-2*H*-cyclopenta[*d*]pyridazine (9).—To a cold (ice bath) solution of 613.4 mg (5.7 mmol) of **1** and 3 ml of triethylamine in 25 ml of dichloromethane and 25 ml of chloroform was added slowly 3 ml of trifluoroacetic anhydride. The mixture was allowed to come to room temperature and stand for 24 hr. Triethylamine (4 ml) and trifluoroacetic anhydride (2 ml) were added. After 7 days the solvent was removed (vacuum) and the residue was chromatographed on a 2 × 10 in. silica gel column. Elution with dichloromethane and then chloroform developed several closely spaced fluorescent (uv light) bands which were collected by final elution with acetone. Chromatography of the residue from the acetone eluate on a 2 × 14 in. silica gel column and elution with chloroform developed four bands, which were removed with 1:10 acetone–chloroform. The major (most polar) band yielded 339.4 mg (49%) of **9** as a yellow solid, mp 175–178°. Recrystallization from dichloromethane gave the analytical sample: mp 178–178.5°; uv max (dry ether) 243 nm (ε 30,500), 287 (sh, 11,100), 294 (11,700), 327 (10,000), and 398 (10,600); nmr (acetone) δ 9.67 (s, 1), 9.11 (s, 1), 7.88 (m, 1), and 6.85 (d, 1).

Anal. Calcd for $C_9H_5N_2OF_3$: C, 50.47; H, 2.34; N, 13.08. Found: C, 50.59; H, 2.28; N, 12.92.

5,7-Bis(trifluoroacetyl)-2-phenyl-2*H*-cyclopenta[*d*]pyridazine (10).—To a cold (ice bath) solution of 109 mg (0.562 mmol) of **3** and 0.3 ml of triethylamine in 15 ml of dichloromethane was added slowly with stirring 0.3 ml of trifluoroacetic anhydride, and

(15) We wish to thank Allan R. Banks and Lucinda Hickernell for performing this experiment.

the mixture was then allowed to come to room temperature. Another 0.5 ml of triethylamine and 0.3 ml of trifluoroacetic anhydride were added after 1 day, and another 0.5 and 0.3 ml of the anhydride after 3 and 4 days, respectively. After 5 days the mixture was chromatographed on a 0.75 × 8 in. silica gel column. The fluorescent (uv light) eluate (dichloromethane) yielded a yellow solid which, after recrystallization from aqueous acetone, gave 159.6 mg (74%) of **10** as yellow needles: mp 181–182°; uv max (dry ether) 258 nm (ε 15,700), 293 (38,100), 345 (10,500), and 392 (11,000).

Anal. Calcd for $C_{17}H_8N_2O_2F_6$: C, 52.85; H, 2.09; N, 7.26. Found: C, 53.04; H, 2.20; N, 7.45.

5,7-Diacetyl-2-methyl-2*H*-cyclopenta[*d*]pyridazine (11).—To a solution of 0.36 ml (3.1 mmol) of anhydrous stannic chloride in 5 ml of acetic anhydride was added a solution of 47.3 mg (0.358 mmol) of **2** in 2 ml of dichloromethane, whereupon the mixture rapidly turned red-brown. After 90 min the mixture was poured into a mixture of 70 ml of 2 *N* NaOH, 50 ml of dichloromethane, and 50 g of ice. The whole was shaken, the layers were separated, and the aqueous layer was extracted with six 35-ml portions of dichloromethane. The solvent was removed (vacuum) from the combined, dried organic solutions and the residue was chromatographed on a 6 × 8 in. silica gel plate using ether and then 3:1 ether–95% ethanol as eluents. The second (more polar) of two fluorescent (uv light) bands yielded a tan solid, which after trituration with a small amount of 95% ethanol and filtration gave 29.9 mg (38.7%) of **11** as a yellow solid: mp 221–224° before and 222–225° after vacuum (*ca.* 10^{-3} mm) sublimation; uv max (dry ether) 225 nm (sh, ε 17,000), 274 (34,000), 291 (11,000), 342 (5600), and 384 (3600); nmr (DMSO) δ 9.62 (s, 1), 9.46 (s, 1), 8.21 (s, 1), and 4.32 (s, 3).

Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.67; H, 5.56; N, 12.95. Found: C, 66.65; H, 5.70; N, 12.83.

Methyl 2-Methyl-2*H*-cyclopenta[*d*]pyridazine-7-carboxylate (13).—A mixture of 98.9 mg (0.434 mmol) of **5**, 4 ml of 10% NaOH, and 2 ml of 95% ethanol was refluxed for 1.75 hr. After it cooled to room temperature, the yellow solution was poured into 20 ml of H_2O and the whole was extracted with three 10-ml portions of ether. Acidification of the cold (ice) aqueous phase with concentrated hydrochloric acid formed a yellow precipitate, which was collected (filtration), washed with H_2O, and dried (vacuum) to yield 83.6 mg of the carboxylic acid **12** as a yellow solid, mp 223–224.5° dec. Attempts to recrystallize **12** from acetone or 95% ethanol gave material having a lower melting point and containing **2** (isolated by extraction of a basic solution with ether and identified by uv and visible spectra).

To a mixture of 123 mg of **12**, 10 ml of dichloromethane, and 10 ml of methanol was added slowly a solution of diazomethane (from 316 mg of *N*-methyl-*N*-nitrosourea)[16] in 5 ml of dry ether. After the acid had been allowed to react, the solution was poured into 10 ml of dilute acetic acid and the separated aqueous layer was extracted with two 10-ml portions of dichloromethane. The residue from the combined, washed (10 ml of 5% sodium bicarbonate and 10 ml of saturated NaCl), dried (sodium sulfate) organic layers was chromatographed on a preparative silica gel G plate. Elution of the least polar band with dichloromethane gave **13** as a yellow solid, mp 109–112°, which after sublimation at 60° (10^{-3} mm) amounted to 72.1 mg (74%) of material: mp 111.2–112.5°; uv max (dry ether) 237 nm (ε 28,600), 253 (22,000), 257 (20,400), 276 (12,300), 282 (12,700), 321 (10,000), and 392 (3470); nmr (acetone) δ 8.96 (broad s, 1), 8.52 (d, 1, *J* = 1.2 Hz), 7.52 (d, 1, *J* = 3.7 Hz), 6.43 (d of d, 1, *J* = 3.7 and 0.7 Hz), and 4.17 (s, 3); ir ($HCCl_3$) 1692 cm^{-1} (C=O).

(16) F. Arndt, "Organic Syntheses," Collect. Vol. II, A. H. Blatt, Ed., Wiley, New York, N. Y., 1943, p 165.

Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30. Found: C, 62.81; H, 5.48.

2-Methyl-2*H*-cyclopenta[*d*]pyridazine-5,7-dicarboxylic Acid (14).—A solution of 280.4 mg (0.865 mmol) of **8** in 20 ml of 95% ethanol and 15 ml of 10% NaOH was heated on a steam bath until no **8** (tlc analysis) remained (3.5 hr). The cooled, stirred solution was acidified slowly with concentrated hydrochloric acid and the precipitate was collected (filtration) and dried (vacuum over P_2O_5) to give **14** as a gray solid which became purple at 200–220° and then black but did not melt below 275°: uv max (0.1 *N* NaOH) 255 nm (ε 33,000), 270 (sh, 24,000), 281 (sh, 7000), 322 (6800), and 372 (sh, 2500); uv max (ether) 282 nm (1.39), 329 (0.76), 374 (0.37), and on dilution 253 (0.55), 269 (0.25), and 282 (0.17).

Anal. Calcd for $C_{10}H_8N_2O_4$: C, 54.54; H, 3.67; N, 12.18. Found: C, 54.37; H, 3.68; N, 12.51.

Dimethyl 2-Methyl-2*H*-cyclopenta[*d*]pyridazine-5,7-dicarboxylate (15).—An excess of diazomethane in ether was added slowly to a stirred suspension of 79.3 mg (0.361 mmol) of **14** in 20 ml of methanol. After 30 min, the excess diazomethane was decomposed (dilute hydrochloric acid) and the solution was then poured into a mixture of 75 ml of H_2O and 30 ml of chloroform. The whole was shaken well and the separated aqueous layer was extracted with two 25-ml portions of chloroform. The residue from the combined, dried organic layers was chromatographed on a 0.75 × 3 in. silica gel column using chloroform and then acetone as eluents. The fluorescent (uv light) band gave 87.3 mg (97.8%) of **15** as a pale tan solid, mp 179–180°. Recrystallization by adding petroleum ether to a concentrated dichloromethane solution formed cream-colored microcrystals: mp 180–180.5°; uv max (dry ether) 253 nm (ε 43,900), 268 (22,300), 280 (12,000), 329 (6120), and 371 (3260); nmr ($DCCl_3$) δ 9.58 (d, 1, *J* = 1 Hz), 9.30 (d, 1, *J* = 1 Hz), 8.28 (s, 1), 4.36 (s, 3, NMe), 3.93 (s, 3, CO_2Me), and 3.91 (s, 3, CO_2Me).

Anal. Calcd for $C_{12}H_{12}N_2O_4$: C, 58.10; H, 4.84; N, 11.30. Found: C, 58.00; H, 4.90; N, 11.13.

Conversion of 7-Trifluoroacetyl-2*H*-cyclopenta[*d*]pyridazine (9) to 7-Trifluoroacetyl-2-methyl-2*H*-cyclopenta[*d*]pyridazine (5).—A mixture of 44.2 mg (0.206 mmol) of **9**, 3 g of BaO, 5 ml of methyl iodide, and 5 ml of dimethyl sulfoxide was shaken occasionally for 24 hr while protected from moisture. Dichloromethane (100 ml) and H_2O (75 ml) were added and the whole was shaken well and filtered (suction). The solid was washed with 25 ml of H_2O and then 25 ml of dichloromethane, and the filtrate was then made slightly acidic with dilute hydrochloric acid and shaken well. The tan residue from the separated, washed (two 100-ml portions of H_2O), and dried organic layer was chromatographed on a 6 × 8 in. silica gel plate using dichloromethane and then 3:2 dichloromethane–petroleum ether as eluents. The second (more polar) fluorescent (uv light) band gave a yellow solid, mp 145–155°, which after recrystallization from aqueous acetone afforded 7.4 mg (18%) of **5** as tiny yellow needles, mp 127–129°, uv and visible spectra identical with those of an authentic sample.

Registry No.—**4**, 32377-07-4; **5**, 35426-58-5; **6**, 35426-59-6; **8**, 35426-60-9; **9**, 35426-61-0; **10**, 35426-62-1; **11**, 35426-63-2; **12**, 35426-64-3; **13**, 35426-65-4; **14**, 35454-84-3; **15**, 35426-66-5; trifluoroacetic anhydride, 407-25-0.