atom complexed to an amide. However, chlorination of 2,3-dimethylbutane by Cl_2, $h\nu$ in the presence and absence of *N*-(1,1-dimethylpentyl)acetamide (0.09 *M*) showed no change in selectivity (k_t/k_p = 3.96 ± 0.08 vs. 3.92 ± 0.08). Other possibilities for species of the composition amidyl radical–HCl can be formulated. In the absence of additional evidence, further discussion is not warranted. It is worth stressing, however, that the selectivity with **2a** in hydrogen abstraction is considerably greater, and the rate of decomposition is faster, under these conditions ($h\nu$, degassed) than in the presence of oxygen or trimethylpyridine. Some high selectivities observed in chlorinations with *N*-chlorosuccinimide[13] may also be associated with complexities of the type described here.

Experimental Section

The preparation and characterization of the *N*-chloro amides and their amide products have been described, as have procedures for decomposition and columns for GLC analysis.[1a] The reaction solutions were directly analyzed by GLC after complete disappearance of the *N*-chloro amide. Typical retention times (in minutes) using column C[1a] (column temperature 60°, flow rate 60 ml/min) follow: 2-chloro-2,3-dimethylbutane (4.3), 1-chloro-2,3-dimethylbutane (5.9), chlorobenzene (7.7), chlorocyclohexane (10.3), *N*-*tert*-butylacetamide (14.7), and 2,4,6-trimethylpyridine (21.5). The products were stable to reaction and GLC analysis conditions, and were identified by comparison with authentic samples.

The chlorination products of *n*-hexane were analyzed on column D.[1a] The 2- and 3-chlorohexanes were not separable and formed a single symmetrical peak. The products were identified by comparison with authentic samples.

The chlorination products of 2,2-dimethylbutane were identified by comparison with authentic samples obtained from the photochlorination with Cl_2. The alkyl chlorides were collected by preparative GLC and structural assignments were made from the NMR spectra. A commercial sample of 4-chloro-2,2-dimethylbutane (Eastman) was also available. 1-Chloro-2,2-dimethylbutane: δ 0.83 (m, 3 H, CH_2CH_3), 0.93 [s, 6 H, $(CH_3)_2C$–], 1.29 (m, 2 H, CH_2CH_3), and 3.25 ppm (s, 2 H, $-CH_2Cl$). 3-Chloro-2,2-dimethylbutane: δ 1.00 [s, 9 H, $(CH_3)_3C$–], 1.40 (d, *J* = 7 Hz, 3 H, $-CHClCH_3$), and 3.80 ppm (q, *J* = 7 Hz, 1 H, $-CHClCH_3$). 4-Chloro-2,2-dimethylbutane: δ 0.93 [s, 9 H, $(CH_3)_3C$–], 1.70 (m, 2 H, $-CH_2CH_2Cl$), and 3.47 ppm (m, 2 H, $-CH_2CH_2Cl$).

Products from the chlorination of adamantane in 2,3-dimethylbutane were analyzed with column C.[1a] An authentic sample was used to identify 1-chloroadamantane, which had a shorter retention time than 2-chloroadamantane, as reported.[7]

The conditions and results are summarized in Tables I–VII.

Registry No.—**1a,** 5014-39-1; **2a,** 10271-73-5; *n*-hexane, 110-54-3; cyclohexane, 110-82-7; 2,3-DMB, 79-29-8; 2,2-DMB, 75-83-2; adamantane, 281-23-2; TMP, 108-75-8; DBPO, 94-36-0; oxygen, 7782-44-7; TCE, 79-01-6; Cl_2, 7782-50-5; 1-chloro-2,2-dimethylbutane, 6366-35-4; 3-chloro-2,2-dimethylbutane, 5750-00-5; 4-chloro-2,2-dimethylbutane, 2855-08-5.

References and Notes

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(5) Trichloroethylene (ref 4) has a much smaller effect on reactivity (see Table I).
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(7) (a) G. W. Smith and H. D. Williams, *J. Org. Chem.*, **26**, 2207 (1961). (b) High discrimination between the tertiary and secondary positions of adamantane has also been observed with $Cl_3C\cdot$ [I. Tabushi, Y. Aoyama, S. Kojo, J. Hamuro, and Z. Yoshida, *J. Am. Chem. Soc.*, **94**, 1177 (1972)] and with photoexcited biacetyl [I. Tabushi, S. Kojo, and Z. Yoshida, *Tetrahedron Lett.*, 2329 (1973)] and attributed, in part, to steric effects.
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(11) S. J. Cristol and H. W. Mueller, *J. Am. Chem. Soc.*, **95**, 8489 (1973).
(12) The similarity in selectivity with **1a** in the presence and absence of the base may be fortuitous; the hydrogen-abstracting species need not be the same under the two conditions.
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2*H*-Cyclopenta[*d*]pyridazines. Electrophilic Halogenation[1,2]

Arthur G. Anderson, Jr.,* David M. Forkey,[3] Larry D. Grina,[4] Lucinda W. Hickernell,[5] Taran Tober, and Max T. Wills

Department of Chemistry, University of Washington, Seattle, Washington 98195

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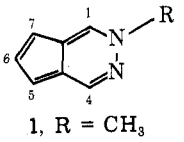
2-Methyl- and 2-phenyl-2*H*-cyclopenta[*d*]pyridazine (**1** and **2**) and the parent system (**3**) undergo electrophilic halogenation with *N*-halosuccinimides. The 5-, 7-, 5,7-, and 5,6,7-chloro and bromo derivatives, the 5,7-iodo derivative, and the 5-trifluoroacetyl-7-bromo and 5-bromo-7-trifluoroacetyl derivatives of **1** were prepared. Based on product yields, the relative position reactivities are 7 > 5 ≫ 6. Dipyridineiodonium nitrate was used to prepare the 5,6,7-triiodo derivative of **1**. The 5-, 7-, 5,7-, and 5,6,7-chloro derivatives of **2** and the 7-chloro and 5,7-dichloro derivatives of **3** were also obtained. The substituent long-wavelength spectral shifts for halogen and trifluoroacetyl were found to be qualitatively additive.

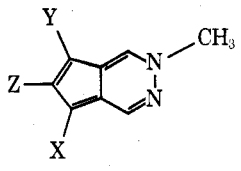
The preceding papers established the positions of protonation[6] and acylation[7] on the 2*H*-cyclopenta[*d*]pyridazine system for mono- and disubstitution. In the present study, electrophilic mono-, di-, and trihalogenation are reported for this heteroanalog of azulene containing both π-excessive and π-equivalent ring nitrogens.



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

Chlorination of 1. As with azulene and cyclopenta-

[c]thiapyran,[8,9] the 2H-cyclopenta[d]pyridazine ring was found to react rapidly with N-halosuccinimides under mild conditions. The 2-methyl compound (1) was especially reactive, and it was necessary to employ an excess of 1 in the reaction with NCS[10] to obtain the monosubstitution products 4 and 5. These compounds (especially 4) were difficult



4, X = Cl; Y = Z = H
5, Y = Cl; X = Z = H
6, X = Y = Cl; Z = H
7, X = Y = Z = Cl
8, Y = Br; X = Z = H
9, X = Y = Br; Z = H
10, X = $COCF_3$; Y = Z = H
11, X = $COCF_3$; Y = Br; Z = H
12, Y = $COCF_3$; X = Z = H
13, X = Br; Y = $COCF_3$; Z = H
14, X = Y = Z = Br
15, X = Y = Cl; Z = Br
16, X = Y = I; Z = H
17, X = Y = Z = I

to separate from each other and from other impurities present and were somewhat unstable, particularly when impure. Complete purification was ultimately accomplished, after many attempts with other methods, by high-pressure liquid chromatography.

The structural assignments for 4 and 5 were determined by analogy with the characteristics found for the corresponding trifluoroacetyl compounds[6,11] and the 7-bromo compound (see below). Thus the major product, and the one for which the NMR chemical shift (δ) for H-4 was relatively larger than for H-1 and for which J for the vicinal five-ring hydrogen coupling was smaller (as would be expected if the non-charge-separated resonance structure is more important than the others), was designated to be the 7 isomer (5). This is also consistent with the major product arising from the intermediate for which the resonance structures indicate the greater stabilization,[6,9] and for which the π-electron localization energy is calculated to be the smaller.[11]

The by-product from the monochlorination was the 5,7-dichloro derivative 6, which was formed in high yield when slightly more than 2 equiv of NCS was used. The NMR spectrum for 6 shows a clean singlet at δ 6.95 for H-6 and peaks at δ 8.69 (H-1) and 8.51 (H-4).

1,3-Dichloroazulene undergoes further electrophilic substitution at the 5 position[12] and the formylation of 1,3-dialkylazulenes has been found to occur at both the 2 and 5 positions.[13] In contrast, attempts to effect the trichlorination of the π-excessive cyclopenta[c]thiapyran gave only polymer-like material. Compounds 1–3 have no substitutable atom corresponding to the 5 position of azulene, so trisubstitution, if it could be accomplished, would be expected to occur at the 6 position (corresponding to the azulene 2 position). Allowing 1 to react with an excess of NCS for a longer period of time gave a good yield of 7 which exhibited NMR peaks at δ 8.99 (H-1), 8.69 (H-4), and 4.34 (NCH_3). Further reaction of 6 with NCS also afforded 7. In the latter reaction, it was essential that 6 be pure and that an excess of NCS be avoided.

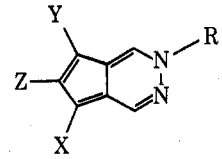
The presence of two trifluoroacetyl or carbomethoxy groups in the 5 and 7 positions of 1 deactivated the ring system such that treatment with NCS gave no further electrophilic substitution.

Bromination of 1. Reaction of 1 with 1 equiv of NBS gave a mixture of products. A low yield (11% based on NBS) of the 7-bromo compound (8) was obtained as an unstable oil. The identity of this material was shown by its NMR spectrum [singlets at δ 8.61 (broad, H-4) and 4.17 (NCH_3), doublets at 8.57 (J = 1 Hz, H-1) and 7.15 (J = 3 Hz, H-6), and a doublet of doublets at 6.61 (J = 3 and 1 Hz, H-5)] and its conversion to the stable 5-trifluoroacetyl-7-bromo derivative (11), identical with the product from the bromination of the 5-trifluoroacetyl compound (10). The major product (83% based on NBS) was the 5,7-dibromo compound (9) [NMR singlets at δ 7.17 (H-6) and 4.27 (NCH_3) and doublets at 8.75 (J = 1 Hz, H-1) and 8.54 (J = 1 Hz, H-4)], and some (37%) unchanged 1 was recovered. No substance corresponding to the 5-bromo derivative was detected. This was attributed to the 5-bromo compound being more reactive to disubstitution and also less stable to isolation than the 7-bromo isomer. The formation of 9 in high yield along with the recovery of unchanged 1 when 1 equiv of NBS was used indicates that the monobromo substitution products are comparable in reactivity to 1. Bromination of the 7-trifluoroacetyl compound (12) gave the stable 5-bromo-7-trifluoroacetyl derivative (13) of established structure.[11]

Tribromination of 1 took place readily to give 14 [singlets in the NMR spectrum at δ 8.89 (H-1), 8.57 (H-4), and 4.43 (NCH_3)], and the dichloro compound (6) also underwent bromination at the 6 position to yield 15, which showed NMR peaks (singlets) at δ 9.05 (H-1), 8.73 (H-4), and 4.34 (NCH_3).

Iodination of 1. From the treatment of 1 with 4 equiv of NIS was isolated a yellow solid which rapidly decomposed above 0°. Solutions in organic solvents were more stable and an NMR spectrum [singlets at δ 8.38 (H-1), 8.16 (H-4), 7.16 (H-6), and 4.20 (NCH_3)] consistent with that expected for the 5,7-diiodo compound (16) was obtained. Curiously, attempts to prepare the 5,6,7-triiodo compound (17) from 1 by reaction with excess NIS were not successful; only 16 was found. Yet reaction of 1 with 5 equiv of dipyridineiodonium nitrate produced the more stable 17 in 19% yield. The NMR spectrum for this compound showed singlets at δ 8.77 (H-1), 8.32 (H-4), and 4.26 (NCH_3). The formation of iodine during the reaction was observed, but 16 was found to be inert to iodine so the latter was not involved in the introduction of the third iodine atom.

Chlorination of 2 and 3.[14] The reaction of 2-phenyl-2H-cyclopenta[d]pyridazine (2) with 1 equiv of NCS afforded a mixture from which was isolated 20% of the 5-chloro (18) and 41% of the 7-chloro (19) derivatives. A small amount of the 5,7-dichloro compound (20) was formed. As with 4 and 5, the major monosubstitution product was judged to be the 7 isomer. Compounds 18 and 19 were considerably more stable than 4 and 5. The use of 2 equiv of NCS gave 20 in 90% yield, and further chlorination of 20 afforded 21 (74%).



18, X = Cl; Y = Z = H; R = C_6H_6
19, X = Z = H; Y = Cl; R = C_6H_5
20, X = Y = Cl; Z = H; R = C_6H_5
21, X = Y = Z = Cl; R = C_6H_5
22, X = H; Y = Cl; Z = R = H
23, X = Y = Cl; Z = R = H

Treatment of 3 with 1 equiv of NCS afforded 88% of a monochloro product. This was assigned the 7-chloro structure (22) [NMR absorption at δ 8.75 and 8.85 (H-1 and H-4), 6.82 (H-5) coupled with 7.22 (H-6) (J = 2 Hz), and a broad singlet at 3.0 (N-H)] on the basis that the 7-monosubstitution product is the major one in the established case of trifluoracetylation of 1, and is the exclusive product

Table I
Long-Wavelength Spectral Shifts for Substituted 2*H*-Cyclopenta[*d*]pyridazines

Substituent	λ_{max}[a] (obsd)	$\Delta\lambda_{max}$[a]	λ_{max}[a] (calcd)
2-CH_3[b]	395		
5-Cl-2-CH_3	405	10	
6-Cl-2-CH_3[c,e]			382
7-Cl-2-CH_3	413	18	
5,7-di-Cl-2-CH_3	420	25	423
5,6,7-tri-Cl-2-CH_3	407	12	
5-Br-2-CH_3[c,f]			403
6-Br-2-CH_3[c,g]			380
7-Br-2-CH_3	412	17	
5,7-di-Br-2-CH_3	420	25	
5,6,7-tri-Br-2-CH_3	405	10	
5,7-di-Cl-6-Br-2-CH_3	408	13	405
5-$COCF_3$-2-CH_3[d]	365	−30	
7-$COCF_3$-2-CH_3[d]	403	8	
5,7-di-$COCF_3$-2-CH_3[d]	370	−25	373
5-$COCF_3$-7-Br-2-CH_3	374	−21	382
5-Br-7-$COCF_3$-2-CH_3	415	20	411
5,7-di-I-2-CH_3	416	21	
6-I-2-CH_3[h]			393
5,6,7-tri-I-2-CH_3	414	19	
2-C_6H_5[b]	408		
5-Cl-2-C_6H_5	417	9	
7-Cl-2-C_6H_5	424	16	
5,7-di-Cl-2-C_6H_5	435	27	433
5,6,7-tri-Cl-2-C_6H_5	422	14	
2-H[b]	395		
7-Cl-2-H	403	8	
5,7-di-Cl-2-H	418	23	

[a] Nanometers. [b] Parent system. [c] Not known. [d] Reference 7. [e] Registry no., 55268-31-0. [f] Registry no., 55268-32-1. [g] Registry no., 55268-33-2. [h] Registry no., 55268-34-3.

when the 7-trifluoracetyl-2-methyl compound (**12**) is formed by methylation of the resonance hybrid anion of monotrifluoracetyl-2*H*-cyclopenta[*d*]pyridazine (which could yield either the 5- or 7-isomers or a mixture).[7] Reaction of **3** with 2 equiv of NBS produced the 5,7-dichloro derivative (**23**) in 82% yield.

Substituent Spectral Shifts. One of the unusual properties of substituted azulene compounds is the additivity of the long-wavelength absorption shifts caused by substituent groups. This was first recognized by Plattner for di-, tri-, and polyalkylazulenes[15] and later was shown to hold for a wide variety of other groups, especially in the 1 and 3 positions, by Cowles[16] and Anderson and coworkers.[17] The present results provided the first opportunity to examine this property with a π-excessive heteroanalog of azulene.[18]

Table I lists the long-wavelength spectral shifts observed for the 5- and 7-mono- and 5,7-disubstituted derivatives, and the values for the latter calculated by simple additivity. It is seen that the correlations are quite good, even in the two cases where quite different groups ($COCF_3$ and Br) are involved. Thus, the 2*H*-cyclopenta[*d*]pyridazine ring system retains the azulenic property of the additivity of substituent long-wavelength shifts. Therefore, it is likely that values for the 5,6,7-trisubstituted compounds provide the basis for qualitatively predicting the shifts for the monosubstituted halo derivatives not yet prepared.

The nonequivalent 5 and 7 positions in this ring system apparently respond differently to groups exerting different electronic effects. For example, chlorine or bromine on either position results in a bathochromic shift with that of the 7 position being the greater. The datum for the diiodo-2-methyl compound indicates that iodine behaves in the same manner. In contrast, the 5-trifluoroacetyl group causes a large hypsochromic and the 7-trifluoroacetyl group a small bathochromic shift. The trifluoroacetyl effect is similar to that of halogen, however, in that the shift for the 7 position is more bathochromic than for the 5 position. It is hoped that data from compounds having other groups will show whether or not these results fit a general pattern.

Experimental Section

Melting points are uncorrected. Uv and visible spectra were recorded on a Cary Model 14 recording spectrophotometer. Ir spectra were recorded with a Perkin-Elmer Model 21 instrument. NMR spectra were taken on a Varian Model A-60, T-60, or DA 60-I1 instrument with tetramethylsilane as internal reference. Mass spectra were recorded on an Associated Electrical Industries MS-9. Analyses were performed by A. Barnhardt, Elbach über Engelskircher, Germany; Chemalytics, Inc., Tempe, Ariz.; Midwest Microlab, Inc., Indianapolis, Ind.; or Mr. Dave Harsch, Department of Chemistry, University of Idaho, Moscow, Idaho. Hydrocarbon, acetonitrile, THF, alcohol, DMF, benzene, ether, and dichloromethane solvents were purified and dried prior to use. All other solvents were reagent grade. Petroleum ether was of bp 20–40°. Solvents were removed from reaction solutions with a rotary evaporator at or below room temperature unless otherwise specified.

5- and 7-Chloro-2-methyl-2*H*-cyclopenta[*d*]pyridazine (4 and 5). To a stirred solution of 400 mg (3.4 mmol) of **1** in 30 ml of CH_2Cl_2 was added dropwise a solution of 390 mg (2.9 mmol) of NCS in 20 ml of CH_2Cl_2 over a period of 30 min. The mixture was concentrated under N_2 to a volume of 10 ml and then was chromatographed on a 1.5 × 12 in. column of neutral alumina with 1:3 ether–petroleum ether as the eluate. The yellow eluate was collected as 60 20-ml fractions, the compositions of which were determined with a Waters Associates liquid chromatograph, Model ALC-100, using a 0.125 in. × 6 ft column of Corisil 2. The eluent was 1:4 *n*-hexane–CH_2Cl_2, the flow rate was 54 ml/hr, and the residual time on the column was ca. 35 min. Fractions 1–32, which contained one product, were combined and concentrated to ca. 5 ml volume. This solution was chromatographed on the Waters instrument except using a 0.375 in. × 6 ft Porasil column and a flow rate of 180 ml/hr. The elution time for the major fraction was ca. 2.5 hr with smaller fractions appearing at ca. 1.5 (**6**) and 3 hr (**5**). The major fraction was concentrated and the last few milliliters were then removed under a stream of N_2. Sublimation of the residue at 50° (10^{-4} mm) gave 40 mg (8.9%) of **4** as yellow crystals: mp 60–60.5°; NMR (acetone) slightly broadened singlets at δ 8.60 (H-1) and 8.55 (H-4), doublets at 7.03 (J = 4 Hz, H-6) and 6.63 (J = 4 Hz, H-7), and a singlet at 4.07 (NCH_3) of the corresponding areas; uv (ether) 247 nm (ϵ 26,488), 253 (25,857), 270 (15,767), 277 (sh, 12,610), 312 (4162), 318 (4919), 324 (4450), 332 (5171), and 405 (865).

Anal. Calcd for $C_8H_7N_2Cl$: C, 57.67; H, 4.23; N, 16.82. Found: C, 57.90; H, 4.24; N, 16.43.

Removal of the solvent from the combined fractions 33–54 (the last few milliliters under N_2) gave 270 mg (60%) of crude **5** which was further purified as described for **4**. The elution time was 3 hr with smaller fractions at 2.5 (**4**) and >4 hr (**1**). Further treatment as described for **4** gave 181 mg (40.2%) of **5** as yellow needles: mp 85–86°; NMR (acetone) slightly broadened singlet at 8.92 (H-4), partially resolved doublet at 8.78 ($J \simeq 1$ Hz, H-1), doublets at 7.24 (J = 3 Hz, H-6) and 6.74 (J = 3 Hz, H-5), and a singlet at 4.30 (NCH_3) of the corresponding areas; uv (ether) 248 nm (ϵ 27,800), 253 (27,000), 264 (20,800), 273 (sh, 15,600), 312 (sh, 3500), 317 (3950), 323 (3850), 331 (3850), and 413 (895).

Anal. Calcd for $C_8H_7N_2Cl$: C, 57.67; H, 4.23; N, 16.82. Found: C, 57.72; H, 4.36; N, 16.65.

5,7-Dichloro-2-methyl-2*H*-cyclopenta[*d*]pyridazine (6). A solution of 102.7 mg (0.778 mmol) of **1** and 230 mg (1.73 mmol) of NCS in 25 ml of CH_2Cl_2 was allowed to stand at room temperature for 1 hr. The solvent was removed and the dark green residue was chromatographed on a 6 × 8 in. silica gel (Merck GF-254) plate with CH_2Cl_2 as the eluent. The major band gave 130.3 mg (83.5%) of **6** as a bright yellow solid, mp 111–113°. Recrystallization from

aqueous acetone gave an analytical sample: mp 113–113.5°; NMR (acetone) singlets at δ 6.95 (M-6) and 4.18 (NCH_3) and doublets at 8.69 (J = 1 Hz, H-1) and 8.51 (J = 1 Hz, H-4); uv (ether) 250 nm (ε 26,000), 254 (26,000), 270 (18,000), 318 (sh, 4100), 324 (4900), 329 (sh, 4600), 337 (4900), and 420 (950).

Anal. Calcd for $C_8H_6N_2Cl_2$: C, 47.76; H, 2.98; N, 13.93; Cl, 35.52. Found: C, 47.60; H, 3.02; N, 13.70; Cl, 35.12

5,6,7-Trichloro-2-methyl-2H-cyclopenta[d]pyridazone (7). A. From 1. To a solution of 574 mg (4.25 mmol) of 1 in 15 ml of CH_2Cl_2 was added 1.775 g (13.30 mmol) of NCS. After the exothermic reaction had subsided, the stoppered flask was placed in a freezer for 24 hr. The mixture was then worked up as described for 6 and recrystallization of the yellow-brown solid obtained from the major band from aqueous ethanol gave 843.2 mg (83.5%) of 7 as yellow needles, mp 127–128.5°. The analytical sample was crystallized from aqueous acetone: mp 128–130°; NMR (acetone) singlets at δ 8.99 (H-1), 8.69 (H-4), and 4.34 (NCH_3); uv (ether) 260 nm (ε 31,000), 272 (sh, 19,000), 321 (3900), 336 (3300), and 407 (1100).

Anal. Calcd for $C_8H_5N_2Cl_3$: C, 40.76; H, 2.12; Cl, 45.22. Found: C, 40.71; H, 2.31; Cl, 45.18.

B. From 6. To a stirred mixture of 87 mg (0.5 mmol) of 6 in 15 ml of CH_2Cl_2 under N_2 was added a solution of 68 mg (0.51 mmol) of NCS in 10 ml of CH_2Cl_2 over a period of 30 min. Stirring was continued for an additional 4 hr. The solvent was removed and the residue was chromatographed on a short column of silica gel CG-7. CH_2Cl_2 removed the green by-products and the main yellow band. The concentrate from the latter was rechromatographed on a 12 × 1.5 in. column. CH_2Cl_2–ether (4:1) separated 7 from a small amount of 6. The major band afforded 72 mg (71%) of 7, mp 127–129.5°, identical (NMR) with the product from A.

5,7-Dibromo-2-methyl-2H-cyclopenta[d]pyridazine (9). Over a period of 10 min, 107 mg (0.603 mmol) of NBS was added to a solution of 79.6 mg (0.603 mmol) of 1 in 10 ml of CH_2Cl_2. After 90 min the mixture was worked up as described for 6 except that 2:1 and then 3:2 hexane–CH_2Cl_2 were used for successive elutions. Three fractions separated. The residue from the major, least polar band was sublimed at 50° (10^{-5} mm) and gave 72.6 mg (83% based on N-bromosuccinimide) of 9 as a yellow solid, mp 125–126.5° dec. An analytical sample was obtained by recrystallization from methanol and two sublimations: 125.3–126.5°; NMR (acetone) singlets at δ 7.17 (H-6) and 4.27 (NCH_3) and doublets at 8.75 (J = 1 Hz, H-1) and 8.54 (J = 1 Hz, H-4); uv (ether) 251 nm (ε 24,100), 256 (24,100), 270 (21,800), 320 (sh, 4550), 328 (5670), 339 (5430), and 420 (1170).

Anal. Calcd for $C_8H_6N_2Br_2$: C, 33.14; H, 2.08; N, 9.66. Found: C, 33.27; H, 2.01; N, 9.49.

The residue from the middle fraction after sublimation at 40° (10^{-5} mm) afforded 14.3 mg (11% based on NBS) of an unstable yellow solid partially characterized as 7-bromo-2-methyl-2H-cyclopenta[d]pyridazine (8): mp 87–88° dec; NMR (acetone) singlets at δ 8.61 (broad, H-4) and 4.17 (NCH_3) and doublets at 8.57 (J = 1 Hz, H-1), 7.15 (J = 3 Hz, H-6), and a doublet of doublets at 6.61 (J = 3 and 1 Hz, H-5); uv (ether) 254 nm (ε 28,000), 313 (sh, 4090), 318 (4640), 321 (sh, 4550), 332 (4750), and 412 (1080).

The most polar fraction afforded 29.1 mg (37%) of unchanged 1, mp 129–129.5°.

5,6,7-Tribromo-2-methyl-2H-cyclopenta[d]pyridazine (14). To a solution of 89.4 mg (0.676 mmol) of 1 in 10 ml of CH_2Cl_2 was added over a 10-min period 380.6 mg (2.13 mmol) of NBS. After 35 min, the dark green mixture was chromatographed on a 1 × 1 in. silica gel column using CH_2Cl_2 and then 1:1 CH_2Cl_2–$HCCl_3$ as eluents. Removal of the solvent from the bright yellow fraction gave 137.6 mg (55%) of 14 as a yellow solid which darkened and became green above 165° and melted at 177–178° dec before and after recrystallization from aqueous acetone: NMR (acetone) singlets at δ 8.89 (H-1), 8.57 (H-4), and 4.43 (N-CH_3); uv (ether) 264 nm (ε 30,100), 277 (sh, 23,100), 319 (3990), 337 (3180), and 405 (1190).

Anal. Calcd for $C_8H_5N_2Br_3$: C, 26.02; H, 1.35. Found: C, 26.16; H, 1.50.

5,7-Dichloro-6-bromo-2-methyl-2H-cyclopenta[d]pyridazine (15). A solution of 47 mg (0.234 mmol) of 6 and 136.4 mg (0.766 mmol) of NBS in 8 ml of CH_2Cl_2 formed needles 25 min after mixing. A small amount of acetone was added to dissolve the needles and the solution was chromatographed on a 1 × 5 in. silica gel column with acetone–CH_2Cl_2 as the eluent. Removal of solvent from the yellow and orange fractions gave a yellow-brown oil which was chromatographed on a 6 × 8 in. silica gel preparative plate with 3:2 CH_2Cl_2–petroleum ether as the eluent. The yellow oil from the major band was crystallized from aqueous ethanol and gave 13 mg (19.9%) of 15 as a yellow solid: mp 120–123°; NMR (acetone) singlets at δ 9.05 (H-1), 8.73 (H-4), and 4.34 (NCH_3); uv (ether) 262 nm (ε 26,000), 273 (sh, 17,000), 318 (3,200), 337 (2500), and 408 (940).

Anal. Calcd for $C_8H_5N_2Cl_2Br$: C, 34.29; H, 1.79; Cl, 25.36; Br, 28.57. Found: C, 34.31; H, 1.87; Cl, 25.42; Br, 28.56.

5-Trifluoroacetyl-7-bromo-2-methyl-2H-cyclopenta[d]pyridazine (11). A. From 5-Trifluoroacetyl-2-methyl-2H-cyclopenta[d]pyridazine (10). A mixture of 25.8 mg (0.113 mmol) of 10[7] and 34.3 mg of NBS in 10 ml of CH_2Cl_2 was stirred for 7 hr. The residue after removal of the solvent was chromatographed three times on a 20 × 30 cm silica gel preparative plate with CH_2Cl_2 as the eluent to afford 24.5 mg (74%) of 11 as yellow crystals, mp 213.5–215°. Recrystallization from hexane–CH_2Cl_2 gave an analytical sample: mp 214.5–215°; NMR (acetone, CAT) singlets at δ 9.13 (broad, H-1), 9.33 (broad, H-4) and 4.50 (NCH_3) and a quartet at 7.51 (J = 2 Hz, H-6); uv (ether) 248 nm (D 0.58), 260 (0.43), 267 (0.42), 292 (0.55), 299 (0.63), and 374 (0.29); ir ($HCCl_3$) 1647 cm^{-1}.

Anal. Calcd for $C_{10}H_6ON_2BrF_3$: C, 39.11; H, 1.97. Found: C, 39.05; H, 2.36.

B. From 8. A mixture of 14.3 mg (0.068 mmol) of 8, 3 drops of trifluoroacetic anhydride, 2 drops of triethylamine, and 1 ml of CH_2Cl_2 was allowed to stand for 2 days. Removal of the solvent and chromatography of the residue twice on a 14 × 25 cm silica gel preparative plate with CH_2Cl_2 as the eluent gave 19.7 mg (95%) of 11 as yellow crystals, mp 213–214.5°, which exhibited spectra (uv, ir) identical with those of the product from A.

5-Bromo-7-trifluoroacetyl-2-methyl-2H-cyclopenta[d]pyridazine (13). A solution of 23.4 mg (0.103 mmol) of 7-trifluoroacetyl-2-methyl-2H-cyclopenta[d]pyridazine (12)[7] and 22.7 mg (0.127 mmol) of NBS was stirred for 22 hr. The solvent was removed and the residue was chromatographed on a 25 × 30 cm silica gel preparative plate with CH_2Cl_2 as the eluent. A minor, less polar band was discarded and the major band afforded a yellow solid, mp 185–189°, which after sublimation at 100° (10^{-5} mm) amounted to 30.5 mg (97%) of 13, mp 187.5–189.5°. Recrystallization several times from hexane–CH_2Cl_2 gave an analytical sample: mp 190.5–191.0°; NMR (acetone) singlets at δ 9.42 (broad, H-4) and 4.47 (NCH_3), a doublet at 8.72 (J = 1 Hz, H-1), and a quartet at 7.58 (J = 2 Hz, H-6); ir ($HCCl_3$) 1632 cm^{-1}; uv (ether) 254 nm (ε 29,900), 288 (sh, 4750), 300 (sh, 4270), 339 (4670), and 415 (8180).

Anal. Calcd for $C_{10}H_6ON_2BrF_3$: C, 39.11; H, 1.97. Found: C, 39.42; H, 2.22.

Reaction of 1 with NIS. A solution of 41.9 mg (0.354 mmol) of 1 and 323.9 mg (1.42 mmol) of NIS[19] in 11 ml of CH_2Cl_2 was stirred for 20 min and then chromatographed on a 1 × 3 in. silica gel column using CH_2Cl_2 as the eluent. Removal of the solvent from the yellow band gave a yellow solid which rapidly decomposed above 0°. Solutions of this substance were more stable and exhibited spectra consistent with the structure of 5,7-diiodo-2-methyl-2H-cyclopenta[d]pyridazine (16): NMR (acetone) singlets at δ 8.38 (H-1), 8.16 (H-4), 7.16 (H-6), and 4.20 (NCH_3); uv (ether) 280 nm (sh, D 1.71), 275 (1.78), 258 (1.83), and on concentration 330 (0.99) and 344 (0.88); visible (ether) 416 nm.

5,6,7-Triiodo-2-methyl-2H-cyclopenta[d]pyridazine (17). To a solution of 1.644 g (4.75 mmol) of dipyridineiodine(I) nitrate[20] in 60 ml of $HCCl_3$ was added 105.2 ml (0.891 mmol) of 1. After 30 hr, the solvent was removed and the residue was chromatographed on a 1 × 3 in. silica gel column with CH_2Cl_2 as the eluent. The yellow band which followed the large I_2 fraction was collected and the solvent was removed. Trituration of the brown solid residue with a small amount of acetone, filtration, and washing with two small portions of CH_2Cl_2 gave 79.3 mg (19.3%) of 17 as yellow-brown crystals which darkened when heated but did not melt at 200°: NMR (dimethyl sulfoxide) singlets at δ 8.77 (H-1), 8.32 (H-4), and 4.26 (NCH_3); uv (ether) 271 nm (ε 31,000), 320 (sh, 5000) and 414 (1200).

Anal. Calcd for $C_8H_5N_2I_3$: C, 18.82; H, 0.98; N, 5.50; I. 74.41. Found: C, 18.80; H, 0.98; N, 5.32; I. 74.92.

5- and 7-Chloro-2-phenyl-2H-cyclopenta[d]pyridazine (18 and 19). To a stirred solution of 97 mg (0.5 mmol) of 2 in 20 ml of CH_2Cl_2 was added a solution of 67 mg (0.5 mmol) of NCS in 10 ml of CH_2Cl_2 over a 30-min period under a N_2 atmosphere. The mixture was concentrated to a small volume and then chromatographed on a 0.5 × 6 in. silica gel (CC-7) column with CH_2Cl_2 as the eluent. The concentrate from the yellow band was chromatographed on three 20 × 20 cm preparative silica gel plates with 2:1 CH_2Cl_2–heptane as the eluent. Four bands with R_f values of 0.33 (unchanged 2), 0.50, 0.58, and 0.70 (20) developed with a slight overlap of the middle two. The bands were physically separated.

Rechromatography of the second on a preparative silica gel plate with 5:2 CH_2Cl_2–heptane as the eluent separated a small amount of the third fraction. Crystallization of the second fraction from ether gave 23 mg (20%) of **18**, mp 120–126°. After sublimation at 50° (10^{-3} mm) the yellow-orange crystals melted at 124–126°: NMR (dimethyl sulfoxide) doublets at δ 9.60 (H-1), 8.90 H-4), 7.25 (H-6), and 7.00 (H-7) and a multiplet centered at 7.77 (5 H); uv (ether) 250 nm (ε 20,000), 258 (sh, 17,000), 289 (22,100), 320 (sh, 7500), and 417 (2680).

Anal. Calcd for $C_{13}H_9N_2Cl$: C, 68.27; H, 3.97; N, 12.25. Found: C, 68.07; H, 3.96; N, 12.28.

Rechromatography of fraction 3 combined with the portion separated from fraction 2 on a preparative silica gel plate with 2:1 CH_2Cl_2–heptane effected separation of the major band from small amounts of **18** and **20**. Sublimination at 50° (10^{-3} mm) of the yellow crystals, mp 76–79°, obtained from the major band gave 47 mg (41%) of **19** as yellow crystals: mp 78–79°; NMR (dimethyl sulfoxide) doublets at δ 9.40 (H-4), 8.27 (H-1), 7.30 (H-6), and 6.88 (H-7) and a multiplet centered at 7.77 (C_6H_5); uv (ether) 252 nm (ε 14,500), 259 (sh, 13,900), 287 (23,100), 322 (sh, 4470), and 424 (2100).

Anal. Calcd for $C_{13}H_9N_2Cl$: C, 68.27; H, 3.97; N, 12.25. Found: C, 68.30; H, 4.31; N, 11.78.

5,7-Dichloro-2-phenyl-2*H*-cyclopenta[*d*]pyridazine (20). To a stirred solution of 97 mg (0.5 mmol) of **2** in 20 ml of CH_2Cl_2 was added a solution of 133 mg (1.0 mmol) of NCS in 10 ml of CH_2Cl_2 over a 30-min period. After 1 hr, the mixture was concentrated to a small volume and chromatographed on a 20 × 20 cm preparative silica gel plate with 2:1 CH_2Cl_2–heptane as the eluent. Recrystallization of the solid, mp 102–104°, from the orange band from ether and then sublimation at 50° (10^{-3} mm) gave 120.2 mg (90%) of **20** as orange crystals: mp 109–109.5°; NMR (dimethyl sulfoxide) doublets at δ 9.40 and 8.90 (H-1 and H-4), multiplet centered at 7.77 (C_6H_5), and a singlet at 7.30 (H-6); uv (ether) 253 nm (ε 20,200), 260 (19,200), 290 (30,000), 331 (sh, 7400), and 435 (2660).

Anal. Calcd for $C_{13}H_8N_2Cl_2$: C, 59.35; H, 3.02; N, 10.65. Found: C, 59.50; H, 3.03; N, 10.83.

5,6,7-Trichloro-2-phenylcyclopenta[*d*]pyridazine (21). To a solution of 38 mg (0.2 mmol) of **2** in 10 ml of acetonitrile was added slowly 39 mg (0.29 mmol) of NCS. The progress of the reaction was monitored by TLC on silica gel and 5% ethyl acetate–95% pentane; no **2** was detected after 8 hr. After standing for 24 hr, orange crystals separated. The mixture was placed in a refrigerator overnight. The separated crystals were washed with cold acetonitrile and dried (vacuum desiccator) and this product (mp 179–180°) then sublimed (50°, 10^{-3} mm) to give 32 mg (74%) of **21**: mp 182–182.5°; NMR ($CDCl_3$) multiplet at δ 7.5–8.2 (5 H, C_6H_5) and a doublet at 8.9 (J = 1 Hz, H-1 and H-4); uv (ether) 258 nm (sh, ε 28,400), 265 (30,700), 294 (33,200), 326 (sh, 8100), and 422 (3200).

Anal. Calcd for $C_{13}H_7N_2Cl_3$: C, 52.44; H, 2.35; N, 9.41. Found: C, 52.46; H, 2.70; N, 9.29.

7-Chloro-2*H*-cyclopenta[*d*]pyridazine (22). To a stirred solution of 117 mg (1.0 mmol) of **3** in 50 ml of CH_2Cl_2 was added dropwise a solution of 119 mg (0.9 mmol) of NCS in 20 ml of CH_2Cl_2 over a period of ca. 10 min. The solvent was removed and the residue was chromatographed on a 0.75 × 6 in. column of SilicAR CC-7[21] with CH_2Cl_2 as the eluent. The combined yellow fractions were concentrated to a small volume and the residue was rechromatographed with a Waters Associates liquid chromatograph, Model ALC-100, using a 0.375 in. × 6 ft Porasil column and 93:7 CH_2Cl_2–ether as the eluent. The residual time on the column was ca. 1.5 hr. Small fractions of less polar (**3**) and more polar (**23**) material were discarded. Removal of the solvent from the major band and sublimation of the residue at 50° (10^{-3} mm) gave 120 mg (88%) of **22** as a yellow solid: mp 126–127°; NMR (acetone) closely spaced multiplets at δ 8.85 (H-4) and 8.75 (H-1), doublets at δ 7.22 (J = 2 Hz, H-6) and 6.82 (J = 2 Hz, H-5), and a broad singlet at 3.0 (NH); uv (ether) 244 nm (ε 33,700), 249 (32,300), 252 (19,100), 305 (4700), 312 (5300), 317 (5100), 325 (5400), and 403 (840).

Anal. Calcd for $C_7H_5N_2Cl$: C, 55.10; H, 3.30; N, 18.36. Found: C, 55.32; H, 3.26; N, 18.06.

5,7-Dichloro-2*H*-cyclopenta[*d*]pyridazine (23). A solution of 430 mg (3.22 mmol) of NCS in 50 ml of acetonitrile was added to a solution of 180 mg (1.53 mmol) of **3** in 15 ml of CH_3CN over a period of 20 min. The mixture was stirred at room temperature for 5 hr, at which time a thin layer chromatogram (silica gel, 9:1 CH_2Cl_2–ether) showed only one yellow spot. Removal of the solvent and chromatography of the residue on SilicAR CC-7[21] with CH_2Cl_2 gave **23** as fine, yellow crystals which were unstable in air. Rechromatography twice more with solvent removal under N_2 afforded 147.5 mg (82%) of long, yellow needles which decomposed at 115°; NMR (acetone-d_6) singlets at δ 8.80 (H-1 and H-4) and δ 7.06 (H-6), uv (ether) 248 nm (ε 23,880), 259 (18,080), 271 (sh, 15,510), 311 (sh, 4509), 318 (5230), 324 (5030), 331 (5046), and 418 (832).

Anal. Calcd for $C_7H_4N_2Cl_2$: C, 44.91; H, 2.14; N, 14.97. Found: C, 45.02; H, 2.10; N, 15.28.

Registry No.—**1**, 22291-85-6; **2**, 22291-84-5; **3**, 270-64-4; **4**, 55268-15-0; **5**, 55268-16-1; **6**, 55268-17-2; **7**, 55268-18-3; **8**, 55268-19-4; **9**, 55268-20-7; **10**, 32377-07-4; **11**, 55268-21-8; **12**, 35426-58-5; **13**, 32377-08-5; **14**, 55298-71-0; **15**, 55268-22-9; **16**, 55268-23-0; **17**, 55268-24-1; **18**, 55268-25-2; **19**, 55268-26-3; **20**, 55268-27-4; **21**, 55268-28-5; **22**, 55268-29-6; **23**, 55268-30-9.

References and Notes

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(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.
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