bonding orbital on this oxygen would be destroyed and stabilization due to the exo-anomeric effect would be lost. An interesting test of this possibility would be to look at the 4-*tert*-butyl isomers, where the *tert*-butyl group would be slightly farther away.[18]

It is also of interest to compare the reactivity ratios found in our 2-alkoxytetrahydropyrans with those found in 1,3-dioxanes.[5] In the former case, in going from axial hydrogen to equatorial hydrogen, the molecule loses only the stabilization of one oxygen lone pair,[19] on the ring oxygen (see Figure 1). The exo-anomeric stabilization is still available. On the other hand, a similar change in the 1,3-dioxanes causes the loss of stabilization from both oxygens, since they are both in the ring. Nevertheless, the ratios in the 1,3-dioxanes (ca. 11), using *tert*-butoxyl radical as abstractor, are similar to our ratios for the systems other than **5** and **6**. This appears to be due to the *tert*-butoxyl system being less selective than triplet ketone. Thus, 2-methoxy-6-methyltetrahydropyran (**2**) gave a cis/trans reactivity ratio of 10 using acetophenone at room temperature[4] and a ratio of only 4 using di-*tert*-butyl peroxide at −40 °C.[6]

In conclusion, we feel that the best value for the reactivity ratio between axial and equatorial hydrogens is 10–16, and the dimethyl substituents are best for locking the ring in an undistorted conformation. The previous values, particularly for compound **1**, were too low, presumably due to conformational flexibility. The *tert*-butyl results appear to be anomalous, and the use of this substituent for conformational locking is risky.

Experimental Section

Compounds **3**, **5**, and **6** were available from a previous study.[12] Compound **4** was prepared from **3** by alkoxy exchange according to the method of Eliel and Giza.[14b] A typical irradiation is described below. In the GC analyses for the dimethyl series, tridecane was used as an internal standard and a 3 mm o.d. × 3.5 m column of 5% Carbowax 20M on 60/80 mesh Chromosorb W (AW DCMS) was used. For the *tert*-butyl compounds, pentadecane was the internal standard and a 3 mm o.d. × 2 m column of 5% QF-1 on 80/100 Chromosorb W AW was used. Calculations were based on the averages of at least three injections for each sample. In most cases, replicate analyses were within 0.5% of the mean, although occasionally 1% variations occurred. Uncertainty ranges were calculated on a "worst case" basis. Thus, extreme values for all four terms in eq 1, based on the observed variations, were used to maximize and minimize the function.

Photodegradation of *cis*- and *trans*-6-*tert*-Butyl-2-methoxytetrahydropyran (5). A solution of 25.2 mg of **5** (33% cis), 29.3 mg of benzophenone, and 11.5 mg of pentadecane in 4 mL of spectral grade benzene was placed in a Pyrex test tube. The sample was sealed with a rubber septum, degassed by three freeze–pump–thaw cycles, and the headspace filled with nitrogen. After analysis, the sample was irradiated with a 450-W high-pressure Xenon lamp with stirring for 50 min and, after further analysis, for an additional 40 min at which time consumption of the cis isomer was 76%, while only 1% of the trans isomer was missing. Trans consumption was corrected for a 2.5% yield of trans from cis–trans isomerization. This yield was determined by irradiation of a sample of pure *cis*-**6**. Such correction was not applied to compounds **3** and **4**, since such isomerization was shown previously[4] to occur largely through abstraction from C-6, and in the dimethyl series, this would produce new diastereomers. Indeed, small additional peaks showed up at reasonable positions in the gas chromatograms.

Acknowledgment. R.D.M. would like to thank the Japan Society for the Promotion of Science for a fellowship to allow him to carry out this research at IMS.

Registry No. *cis*-**3**, 79297-69-1; *trans*-**3**, 79233-93-5; *cis*-**4**, 94110-47-1; *trans*-**4**, 94160-55-1; *cis*-**5**, 79233-92-4; *trans*-**5**, 79233-91-3; *cis*-**6**, 16822-20-1; *trans*-**6**, 16831-17-7; benzophenone, 119-61-9.

(18) Jeffrey, G. A. in ref 2a, p 50.

(19) We continue our practice of using hybrid orbitals on oxygen, despite photoelectron spectroscopic results showing two different ionization potentials.[20] Although consideration of p- and s-type orbitals may be useful for explaining the energetics of ionization, which involves primarily the HOMO, we feel that consideration of hybrids is a convenient device which may take into account stabilizing factors from more than one MO in the transition states leading to our radicals.

(20) Sweigart, D. A. *J. Chem. Educ.* **1973**, *50*, 322 and references cited therein.

Unusual Rearrangement and Eliminative Cleavage of a Tetrachloronorbornenecarboxamide[1]

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In connection with a study requiring 2,2-disubstituted 7-methylenenorbornanes, we prepared the tetrachlorodimethoxy endo carboxamide **1**. Our attempts to relate **1** to the corresponding carboxylic acid have led to a base-promoted transformation of unusual complexity and extent, which we now report. Depending on the reaction conditions, **1** is converted either to **5** or to **8** or to a mixture of **5** and **8** (Scheme I). The tricyclic α'-alkoxy lactam **5** is concluded to be a reversibly formed side product in the ultimate transformation of **1** to **8** by ethanolic hydroxide because the ratio of **5** to **8** diminishes with time under the conditions shown and because of the separately observed conversion of isolated **5** into **8** by ethanolic hydroxide.

To account for the first stage of this transformation, the production of **5**, we have postulated the mechanism shown in Scheme II and formulated the exchange **3** → **5** as proceeding through a base-promoted elimination leading to a strained intermediate, **4**. α'-Alkoxy lactams as a class are known[2-4] and, among other synthetic routes, have been shown to result from the corresponding lactamols by acid-catalyzed treatment with alcohols.[3] Such a transformation under acidic conditions may proceed mechanistically through a lactamol's ring-chain tautomer, the keto amide.[3,4] However, our alkaline conditions would seem to offer little opportunity for exchanging α' substituents by opening and reclosing the lactam once it has been established, and the inertness of the corresponding exo carboxamide toward base argues an initiatory role for lactam formation in **1**. One such alkaline mechanism would account for **5** by alkoxide attack on **3** to give **6**, which might then add alkoxide (exo) and reclose. This sequence would avoid "violating" Bredt's rule[5] but appears incompatible with the observed conversion of **5** to **8** by hydroxide in that it predicts extensive saponification and loss of

(1) Taken in part from the Ph.D. Thesis of J.K.W., Rutgers University, 1984.

(2) Toda, M.; Niwa, H.; Ienaga, K.; Hirata, Y. *Tetrahedron Lett.* **1972**, 335.

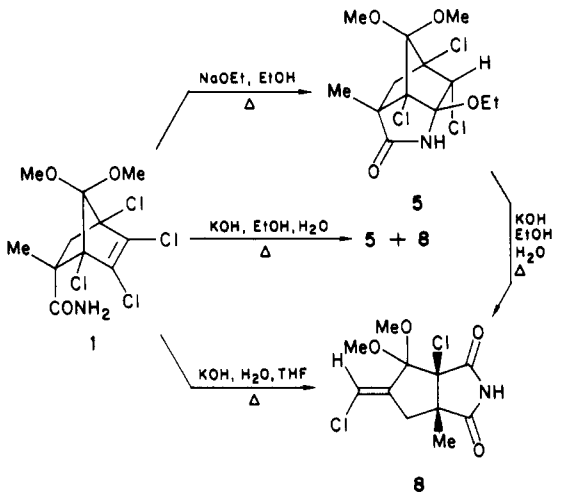
(3) Rodig, O. R.; Johnston, N. J. *J. Org. Chem.* **1969**, *34*, 1942, 1949.

(4) Cromwell, N. H.; Cook, K. E. *J. Am. Chem. Soc.* **1958**, *80*, 4573. Bowers, A. *J. Org. Chem.* **1961**, *26*, 2043. Nagata, W.; Hirai, S.; Itazaki, H.; Takeda, K. *Ibid.* **1961**, *26*, 2413; *Liebigs Ann. Chem.* **1961**, *641*, 184, 196. Nagata, W.; Hirai, S.; Aoki, T.; Takeda, K. *Chem. Pharm. Bull. Jpn.* **1961**, *9*, 845. Meyer, W. L.; Schnautz, N. G. *J. Org. Chem.* **1962**, *27*, 2011.

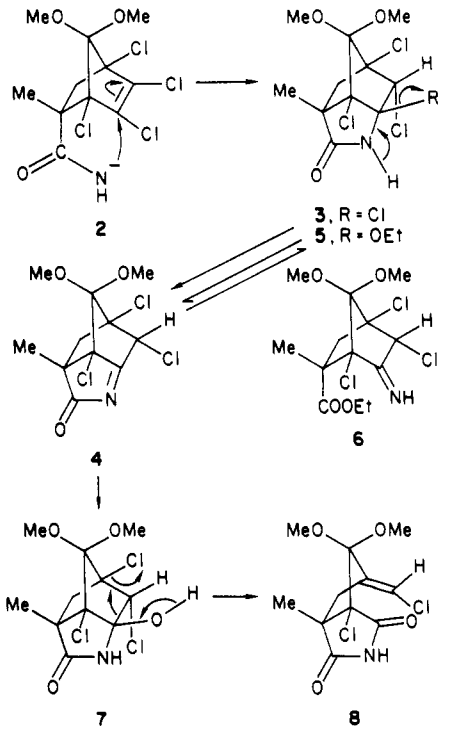
(5) Shea, K. J. *Tetrahedron* **1980**, *36*, 1683 and references cited.

0022-3263/85/1950-0404$01.50/0

Scheme I



Scheme II



nitrogen in that process. In fact, the intermediacy of 4 appears consistent with numerous instances of detected or implied strained intermediates in similar carbocyclic[6] and heterocyclic[7] systems, including at least two eliminations which lead to bridgehead imines and are clearly base initiated.[8]

For the conversion of compound 5 to 8, ethoxide ion alone is inadequate: in contrast to the above-described behavior with hydroxide, treatment of 1 with excess sodium ethoxide in absolute ethanol produced only 5, in 77% isolated yield. Therefore a role for hydroxide in the transformation of 5 to 8 beyond that of mere proton removal is obviously required, and we have formulated this as 5 → 4 → 7 → 8. The survival of 8 is due to anion formation (the pK_a of succinimide is 9.6) and the absence of possibilities for further elimination of chloride. When the desmethyl endo carboxamide 9 was treated with excess aqueous alcoholic base, only product analogous to 5 was isolated, and none corresponding to 8. This result may well have arisen from such further eliminations, prevented in 8 itself by the presence of the methyl group.

In the sequence 1 → 5 the only uncharged intermediate likely to be isolatable is 3. Since the step 1 → 3 is merely catalytic in base, a reaction conducted with an insufficiency of base might provide 3 if the subsequent step 3 → 4, which consumes base, were slow enough. However, when 1 was treated with 0.5 equiv of ethoxide in absolute ethanol, a mixture of 1 and 5 resulted (>85% total isolated yield), with no detectable 3, indicating that step 3 → 4 is fast relative to 2 → 3. An attempt to convert 1 to 3 with potassium *tert*-butoxide in tetrahydrofuran yielded a gross mixture with numerous components.

Experimental Section[9]

Preparation of 1,4,5,6-Tetrachloro-7,7-dimethoxy-*exo*-2-methylbicyclo[2.2.1]hept-5-ene-*endo*-2-carboxamide (1). A mixture of 21.0 g (79.6 mmol) of tetrachloro-5,5-dimethoxycyclopentadiene and 13.8 g (159 mmol) of methacrylamide in 80 mL of absolute EtOH was refluxed for 3 days. Some EtOH was distilled off and the residue was poured into 400 mL of 1:1 water–hexane and shaken. The resulting solid was filtered, dissolved in $CHCl_3$, washed with water and brine, and dried. Concentration provided a crude solid recrystallized from ether–hexane to give 6.5 g (24%) of 1. Further recrystallization give analytically pure material: 177–178 °C; mass spectrum, *m/e* (relative intensity) 318.3 (4.4), 316.0 (34.5), 314.3 (98.9), 312.2 (100), 269.2 (56.7), 267.2 (55.6); IR (Nujol) 3460, 1680, 1600 cm^{-1}; ^1H NMR δ 5.80–5.30 (br, 2 H, exchanges with D_2O), 3.61 (s, 3 H), 3.54 (s, 3 H), 3.17 (d, 1 H, J = 12 Hz, H_{3X}), 2.10 (d, 1 H, J = 12, H_{3N}), 1.62 (s, 3 H). Anal. Calcd for $C_{11}H_{13}Cl_4NO_3$: C, 37.85; H, 3.75; Cl, 40.63; N, 4.01. Found: C, 38.04; H, 3.84; Cl, 40.01; N, 3.80.

This compound was also prepared in 47% yield from the corresponding carboxylic acid, utilizing carbonyldiimidazole.

Conversion of 1 to 3a,5-*endo*-6-Trichloro-6a-ethoxy-4,4-dimethoxy-3-methyl-3,5-methanohexahydrocyclopenta[*b*]-pyrrol-2(1*H*)-one (5) by Ethanolic NaOEt. A suspension of 1.50 g (4.30 mmol) of carboxamide 1 in 23 mL of absolute EtOH was added to a solution produced by dissolving 240 mg (10.4 mmol) of Na in 7 mL of absolute EtOH. When this solution had been refluxed for 5–10 min a white precipitate appeared, and after 30 min TLC showed the absence of 1 and the presence of only 5. After 1 h of reflux, roughly one-half the mixture was worked up by aqueous dilution, Et_2O extraction, and concentration, to provide 800 mg of 5, mp 147–9 °C. Overnight reflux of the remaining reaction mixture produced some brown color and, upon workup, 390 mg of 5, mp 145–8 °C, but no trace of 8 either by TLC or by acidification of the aqueous extracts. The combined isolates,

(6) Nickon, A.; Covey, D. F.; Huang, F.; Kuo, Y.-N. *J. Am. Chem. Soc.* **1975**, *97*, 904.

(7) Grob, C. A.; Sieber, A. *Helv. Chim. Acta* **1967**, *50*, 2531. Toda, M.; Hirata, Y.; Yamamura, S. *Chem. Commun.* **1970**, 1597. Fisher, R. D.; Bogard, T. D.; Kovacic, P. *J. Am. Chem. Soc.* **1972**, *94*, 7599; **1973**, *95*, 3646. Gassman, P. G.; Cryberg, R. L.; Shudo, K. *Ibid.* **1972**, *94*, 7600. Krabbenhoft, H. O.; Wiseman, J. R.; Quinn, C. B. *Ibid.* **1974**, *96*, 258. Kropp, P. J.; Worsham, P. R.; Davidson, R. I.; Jones, T. H. *Ibid.* **1982**, *104*, 3972. Sasaki, T.; Eguchi, S.; Okano, T.; Wakata, Y. *J. Org. Chem.* **1983**, *48*, 4067. Dunkin, I. R.; Shields, C. J.; Quast, H.; Seiferling, B. *Tetrahedron Lett.* **1983**, *24*, 3887.

(8) Reed, J. O.; Lwowski, W. *J. Org. Chem.* **1971**, *36*, 2864. Becker, K. B.; Gabutti, C. A. *Tetrahedron Lett.* **1982**, *23*, 1883.

(9) Melting points were determined with a Thomas-Hoover Uni-Melt apparatus and are uncorrected, as are boiling points. IR spectra were taken on a Perkin-Elmer 727B, 1320, or 180IR spectrometer, by using KBr pellets unless otherwise specified. ^1H NMR spectra were recorded at 60, 79.5, and 90 MHz with Varian T60A, CFT-20, and EM-390 spectrometers, respectively, and at 100 MHz with a Varian XL-100 or a JEOL JNM-PS-FT-100 spectrometer, utilizing $CDCl_3$ ($SiMe_4$) as the solvent. ^{13}C NMR spectra were recorded at 20 and 25.16 MHz with Varian FT-80A and XL-100 spectrometers, respectively, utilizing $CDCl_3$ as solvent unless otherwise specified. Low- and high-resolution mass spectra were determined with Varian CH-5 and MAT312 spectrometers, respectively. Elemental analyses were carried out with a Perkin-Elmer 240 elemental analyzer (C, H, N) and an American Instrument Co. chloride titrator. Reactions were normally run under an atmosphere of N_2, and E. Merck G60 and Baker 60–200-mesh SiO_2 were used for preparative and flash chromatography, respectively.

totaling 77%, were recrystallized from i-Pr_2O to give analytically pure **5**: mp 151–153 °C; CI mass spectrum, m/e (relative intensity) 379.2 ($M^+ + NH_4$, 15.3), 377.1 ($M^+ + NH_4$, 48.0), 375.1 ($M^+ + NH_4$, 51.1), 362.1 (M^+, 31.2), 360.2 (M^+, 94.8), 358.1 (M^+, 100); IR 3500, 1735, 1450 cm^{-1}; ^1H NMR δ 7.15 (br s, 1 H, exchanges with D_2O), 4.55 (d, 1 H, J = 2 Hz), 3.78 (q, 2 H, J = 7), 3.70 (s, 3 H), 3.65 (s, 3 H), 2.41 (d, 1 H, J = 13, H_{7N}), 1.80 (dd, 1 H, J = 13, 2, H_{7X}), 1.34 (s, 3 H), 1.28 (t, 3 H, J = 7); ^{13}C NMR (C_6D_6) δ 177.3 (s), 103.3 (s), 92.5 (s), 81.6 (s), 77.8 (s), 71.9 (s), 71.5 (d), 61.4 (t), 51.7 (q), 50.5 (q), 40.7 (t), 17.7 (q), 15.3 (q). Anal. Calcd for $C_{13}H_{18}Cl_3NO_4$: C, 43.52; H, 5.06; Cl, 29.66; N, 3.91. Found: C, 43.80; H, 5.15; Cl, 29.25; N, 3.84.

Conversion of 1 to a Mixture of 1 and 5 with an Insufficiency of Ethanolic NaOEt. Carboxamide **1** (1.00 g, 2.87 mmol), dissolved in 16 mL of absolute EtOH, was added to a solution prepared by dissolving 33 mg (1.44 mmol, 0.5 equiv) of Na in 7 mL of absolute EtOH. This solution was refluxed for 21 h and monitored by TLC, with no observable change noted after 15 min. Chromatography of the isolated product mixture gave 469 mg (47%) of recovered starting material (**1**) and 395 mg (38%) of **5**, each identical with the corresponding previously described material, no other compounds being isolatable.

Conversion of 1 to 3a-Chloro-(*E*)-5-(chloromethylene)-4,4-dimethoxy-6a-methyl-*cis*-tetrahydrocyclopenta[*c*]pyrrole-1,3(2*H*,3a*H*)-dione (8) by Aqueous KOH. A mixture of 100 mg (0.286 mmol) of carboxamide **1**, 250 mg (4 mmol) of KOH, and 3 mL of 2:1 THF–water was refluxed for 3 h. Extracts of the basic mixture contained **1** and several minor impurities but no significant amount of **5** (TLC); extracts of the acidified mixture were chromatographed to provide 25 mg (30%) of **8**, mp 179–181 °C after recrystallization from i-Pr_2O: mass spectrum, m/e (relative intensity) 297.1 (M^+, 0.91), 295.1 (M^+, 4.5), 293.1 (M^+, 7.2), 266.1 (3.57), 264.1 (20.5), 262.1 (32.8), 260.1 (25.0), 258.1 (75.4), 193.1 (55.2), 191.1 (82.3), 150.1 (78.8), 148.1 (91.5), 113.2 (100); IR 3500, 1790, 1725, 1660 cm^{-1}; ^1H NMR δ 8.15 (br s, 1 H, exchanges with D_2O), 6.45 (dd, 1 H, J = 3, 2 Hz), 3.47 (s, 3 H), 3.17 (s, 3 H), 2.91 (dd, 1 H, J = 18, 3), 2.49 (dd, 1 H, J = 18, 2), 1.45 (s, 3 H); ^{13}C NMR δ 179.4 (s), 171.4 (s), 137.2 (s), 119.4 (d), 107.5 (s), 80.3 (s), 54.7 (s), 51.2 (q), 50.6 (q), 33.6 (t), 23.5 (q). Anal. Calcd for $C_{11}H_{13}Cl_2NO_4$: C, 44.92; H, 4.45; Cl, 24.10; N, 4.76. Found: C, 44.95; H, 4.56; Cl, 23.83, N, 4.78.

Conversion of 1 to a Mixture of 5 and 8 by Ethanolic KOH. A mixture of 2.60 g (7.5 mmol) of carboxamide **1**, 6.50 g (0.1 mol) of KOH and 80 mL of 5:1 EtOH–water was refluxed for 3 h. Workup and separation as outlined above yielded 970 mg (36%) of **5** and 860 mg (39%) of **8**, each identical with the corresponding previously described material. An analogous experiment, carried out for 72 h, gave 4.3% of **5** and 46% of **8**.

Treatment of the exo carboxamide, epimeric with **1**, under similar conditions provided only unchanged starting material.

Conversion of 5 to 8 by Ethanolic KOH. A mixture of 500 mg (1.39 mmol) of lactam **5**, 1.25 g (0.02 mol) of KOH, and 15 mL of 5:1 EtOH–water was refluxed for 46 h. Workup and separation as outlined above yielded 100 mg (20%) of starting material (**5**) and 140 mg (34%) of **8**, each identical with the corresponding previously described material.

Preparation of 1,4,5,6-Tetrachloro-7,7-dimethoxybicyclo[2.2.1]hept-5-ene-*endo*-2-carboxamide (9). A mixture of 11.5 g (43.6 mmol) of tetrachloro-5,5-dimethoxycyclopentadiene and 6.4 g (87.2 mmol) of acrylamide in 20 mL of absolute MeOH was refluxed for 16 h. After cooling, water was added and precipitated material was filtered, washed with water, dried, and recrystallized from i-Pr_2O to afford 10.8 g (75%) of analytically pure, white **9**: mp 157–9 °C; IR 3460, 1685, 1600 cm^{-1}; ^1H NMR δ 5.90 (br, 2 H, exchanges with D_2O), 3.64 (s, 3 H), 3.59 (s, 3 H), 3.21 (dd, 1 H, J = 5, 8 Hz), 2.42 (octet, 2 H). Anal. Calcd for $C_{10}H_{11}Cl_4NO_3$: C, 35.84; H, 3.31; Cl, 42.33; N, 4.18. Found: C, 35.53; H, 3.22; Cl, 42.08; N, 3.93.

Conversion of the Desmethyl Endo Carboxamide (9) to 3a,5-*endo*-6-Trichloro-4,4,6a-trimethoxy-3,5-methanohexahydrocyclopenta[*b*]pyrrol-2(1*H*,3*H*)-one. Carboxamide **9** (2.0 g, 6.0 mmol) and 5.0 g of KOH (0.08 mol) were refluxed in 60 mL of 1:1 MeOH–water for 64 h. Workup as outlined for **5** and recrystallization from Et_2O–hexane gave 600 mg (30%) of fine white crystals: mp 237.5–239 °C; FAB mass spectrum, m/e (relative intensity) 424.3 ($M^+ + 1$ + glycerol, 8.8), 422.4 (9.0), 334.0 (35.0), 332.9 (14.0), 331.9 (79.8), 331.0 (14.5), 330.1 (100); IR 3160, 1720, 1680 cm^{-1}; ^1H NMR δ 7.80 (br s, 1 H), 4.72 (d, 1 H, J = 1.5 Hz), 3.66 (s, 3 H), 3.63 (s, 3 H), 3.53 (s, 3 H), 2.82 (dd, 1 H, J = 10, 2), 2.41 (ddd, 1 H, J = 12.5, 10, 1.5), 2.18 (dd, 1 H, J = 12.5, 2). Anal. Calcd for $C_{11}H_{14}Cl_3NO_4$: C, 39.96; H, 4.27; Cl, 32.17; N, 4.24. Found: C, 39.89; H, 4.17; Cl, 31.95; N, 4.18.

Conversion of the Desmethyl Endo Carboxamide (9) to 3a,5-*endo*-6-Trichloro-6a-ethoxy-4,4-dimethoxy-3,5-methanohexahydrocyclopenta[*b*]pyrrol-2(1*H*,3*H*)-one. Carboxamide **9** (4.0 g, 11.9 mmol) and 10.0 g of KOH (0.16 mol) were refluxed in 120 mL of 5:1 EtOH–water for 3 h. Workup as outlined for **5** provided 1.0 g of white powder from extraction of the basic solution and 150 mg of the same material (mp, mmp, and ^1H NMR) from extraction of the acidified solution (total yield 28%). Recrystallization from i-Pr_2O gave material of mp 204–206 °C; IR (Nujol) 3150, 1720, 1680 cm^{-1}; ^1H NMR δ 7.83 (br s, 1 H), 4.78 (d, 1 H, J = 1.5 Hz), 3.80 (q, 2 H, J = 7), 3.68 (s, 3 H), 3.62 (s, 3 H), 2.84 (dd, 1 H, J = 10.5, 2), 2.46 (ddd, 1 H, J = 12.5, 10.5, 1.5), 2.18 (dd, 1 H, J = 12.5, 2), 1.28 (t, 3 H, J = 7); ^{13}C NMR (C_6D_6) δ 174.8 (s), 102.7 (s), 93.0 (s), 77.8 (s), 72.1 (s), 71.9 (d), 61.3 (t), 51.9 (d), 51.4 (q), 50.6 (q), 32.6 (t), 15.3 (q). Anal. Calcd for $C_{12}H_{16}Cl_3NO_4$: C, 41.82; H, 4.68; Cl, 30.91; N, 4.07. Found: C, 41.95; H, 4.69; Cl, 30.52; N, 3.91.

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Registry No. **1**, 94294-31-2; **5**, 94294-32-3; **8**, 94323-92-9; **9**, 94294-33-4; acrylamide, 79-06-1; tetrachloro-5,5-dimethoxycyclopentadiene, 2207-27-4; methacrylamide, 79-39-0; 3a,5-*endo*-6-trichloro-4,4,6a-trimethoxy-3,5-methanohexahydrocyclopenta[*b*]pyrrol-2(1*H*,3*H*)-one, 94294-34-5; 3a,5-*endo*-6-trichloro-6a-ethoxy-4,4-dimethoxy-3,5-methanohexahydrocyclopenta[*b*]-pyrrol-2(1*H*,3*H*)-one, 94294-35-6.

A New Synthesis of Isoguanosine

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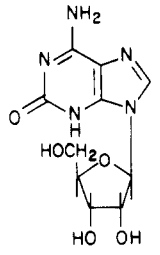
Isoguanosine (**1**) (crotonoside or 2-hydroxyadenosine) is one of only a few naturally occurring nucleoside analogues of guanosine.[1] It was first isolated from *Croton*



1

tiglium L. by Cherbuliez and Bernhard.[2] More recently, Pettit and his co-workers isolated isoguanine from butterfly wings of *Prioneris thestylis*.[3] Isoguanosine is incorporated in mammalian but not bacterial nucleic acids.[4,5] It stim-

(1) Suhadolnik, R. J. "Nucleosides as Biological Probes", Wiley: New York, 1979; p 60.
(2) Cherbuliez, E.; Bernhard, K. *Helv. Chim. Acta* **1932**, *15*, 464, 978.
(3) Pettit, G. R.; Ode, R. H.; Coomes, R. M.; Ode, S. L. *Lloydia* **1976**, *39*, 363.

0022-3263/85/1950-0406$01.50/0