Nuclear magnetic resonance spectra were obtained on a JOEL FX-90 Q spectrometer operating at 22.5 MHz for carbon (Me_4Si), 84.7 MHz for fluorine ($CFCl_3$), and 89.8 MHz for proton ($CDCl_3$) in either $CDCl_3$ on acetone-d_6 solutions. HPLC separations were accomplished on a Perkin-Elmer series LC-1 system with a Perkin-Elmer LC-75 spectrophotometric detector and a Whatman Partisil M9 10/50 or Whatman Partisil M9 10/50 ODS-2 column with HPLC grade solvents as specified. Mass spectra were obtained by Rich Berger at the Washington University School of Medicine, St. Louis. Melting points were obtained on a Thomas-Hoover capillary apparatus.

General Procedure. Cesium fluoroxysulfate (1 mmol) was added to 25 mL of dry acetonitrile in a small plastic vial, and the resulting solution was flushed with nitrogen for several minutes. The aromatic compound (1 mmol) was added to the stirred solution, and the solution was flushed again with nitrogen. Four drops of boron trifluoride etherate were added, and the vial was closed, wrapped in aluminum foil, and allowed to stir for 3 h in the dark, at which time an additional 1 mmol of cesium fluoroxysulfate was added to the solution. The vial was again closed, wrapped in aluminum foil, and allowed to stir for 3 more h for highly activated aromatic compounds or overnight for the less activated aromatic compounds. The solution was transferred to a large test tube and placed on a centrifuge for 2 min. The liquid was decanted and evaporated on a Büchi evaporator. The crude product was transferred to a smaller flask, using acetone, in which the cesium salts are insoluble, and the acetone was evaporated. The crude product was placed under vacuum to remove all remaining traces of solvent. The crude product was first analyzed by ^{19}F NMR.

Resorcinol (1). Two monofluorination products were isolated by HPLC on a Partisil M9 10/50 column with a 2:1 mixture of hexane–ethyl acetate at a flow rate of 4 mL/min. 2-Fluororesorcinol (**2**) was obtained as an oil (64%): ^1H NMR (acetone-d_6) δ 8.31 (OH), 6.66 (m, 1 H), 6.32 (m, 2 H); ^{19}F NMR ϕ −139.8 ppm; mass spectrum, m/e calcd 128, found 128. Anal. Calcd for $C_6H_5FO_2$: C, 56.25; H, 3.91. Found: C, 56.20; H, 3.73. 4-Fluororesorcinol (**3**): mp 98–99 °C (32%); ^1H NMR (acetone-d_6) δ 8.29 (s, 2 H, OH), 6.26–6.90 (m, 3 H, Ar); ^{13}C NMR (acetone-d_6) δ 105.6 (J_{CF} = 2.4 Hz), 106.8 (J_{CF} = 6.1 Hz), 116.6 (J_{CF} = 19.5 Hz) 145.6 (J_{CF} = 229.5 Hz), 146.1 (J_{CF} = 14.6 Hz), 155.0 (J_{CF} = 0 Hz) ppm; ^{19}F NMR (acetone-d_6) ϕ −145.88 ppm; mass spectrum, m/e calcd 128, found 128. Anal. Calcd for $C_6H_5OF_2$: C, 56.25; H, 3.91. Found: C, 56.35; H, 3.77.

17β-Estradiol (4) produced two products, which were isolated by HPLC on a Partisil M9 10/50 ODS-2 column with a 10:1.1:1 mixture of hexane–methylene chloride–isopropyl alcohol at a flow rate of 2.5 mL/min. 2-Fluoro-17β-estradiol (**5**) (20%): mp 174–175 °C (lit.[8] mp 173–175 °C); ^{19}F NMR ϕ −138.4 (d) ppm. 4-Fluoro-17β-estradiol (**6**) (20%): mp 189–190 °C (lit.[8] mp 189–191 °C); ^{19}F NMR ϕ −137.0 (m) ppm. Both **5** and **6** were characterized by comparison with authentic samples.[8]

2-(*N*-Acetylamino)naphthalene (7) produced, after column chromatography on alumina with methylene chloride, 1-fluoro-2-(acetylamino)naphthalene (**9**, R = NHAc) (58%) [mp 118–120 °C (lit.[1] mp 120–121 °C); ^{19}F NMR ϕ −141.7 ppm] and 1,1-difluoro-2-oxo-1,2-dihydronaphthalene (**10**) (21%) [mp 49–50 °C (lit.[1] mp 49–50); ^{19}F NMR ϕ −101.5 ppm].

2-Hydroxynaphthalene (8) produced **9** (R = OH) (50%), mp 74–75 °C (lit.[1] mp 74–75 °C), and **10** (13%).

9-(*N*-Acetylamino)phenanthrene (11) gave after purification on alumina (benzene), 9,9-difluoro-10-oxo-9,10-dihydrophenanthrene (**12**) (22%): mp 93–94 °C (lit.[2] mp 100–102 °C); ^{19}F NMR ϕ −103.6 ppm.

9-(*N*-Acetylamino)anthracene (13) gave only 9,10-anthraquinone (**14**) (75%), mp 283–284 °C (authentic sample mp 283–284 °C).

5-(*N*-Acetylamino)benzo[*c*]phenanthrene (15) and 5-hydroxybenzo[*c*]phenanthrene (16)[14] gave, after chromatography on alumina (benzene), 6,6-difluoro-5-oxo-5,6-dihydrobenzo[c]phenanthrene (**17**) in 10% and 24% yields, respectively: mp 93–94 °C; ^1H NMR ($CDCl_3$) δ 7.47–8.64 (m, Ar); ^{19}F NMR ϕ −110.7 ppm; ^{13}C NMR ($CDCl_3$) 108.5 (t, J = 246 Hz) 121.5, 126.1, 126.7, 128.3, 128.7, 129.5, 130.6, 181.4 (C=O) ppm; mass spectrum, m/e calcd 280, found 280. Anal. Calcd for $C_{18}H_{10}FO_2$: C, 77.14; H, 3.57. Found: C, 77.01; H, 3.72.

Registry No. **1**, 108-46-3; **2**, 103068-40-2; **3**, 103068-41-3; **4**, 50-28-2; **5**, 16205-32-6; **6**, 1881-37-4; **7**, 581-97-5; **8**, 135-19-3; **9** (R = NHAc), 19580-15-5; **9** (R = OH), 51417-63-1; **10**, 51417-64-2; **11**, 4235-09-0; **12**, 59830-28-3; **13**, 37170-96-0; **14**, 84-65-1; **15**, 4176-51-6; **16**, 38063-26-2; **17**, 103068-42-4; $CsSO_4F$, 70806-67-6; piperonal, 120-57-0.

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Synthesis of Volatile, Fluorescent 7-Methylguanine Derivatives via Reaction with 2-Substituted Fluorinated Malondialdehydes

Gabriele Sabbioni and Steven R. Tannenbaum*

Department of Applied Biological Sciences, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

David. E. G. Shuker

M.R.C. Toxicology Unit, Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey SM5 4EF, England

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Many carcinogens that are alkylkating agents react with DNA to give a wide range of alkylated purine and pyrimidine bases. Carcinogenic methylating agents such as methyl methanesulfonate (MMS), *N*-methyl-*N*-nitrosourea (MNU), and dimethylnitrosamine (DMN) give rise to 7-methylguanine (7-MeG) as the major product of reaction with DNA and other nucleic acids.[1] Thus, the determination of 7-MeG in physiological fluids and tissues is of major importance given the wide range of methylating agents to which man may be exposed.

The analysis of 7-MeG or related compounds is made particularly difficult by the chemical properties of naturally occurring purines. Guanine and its alkylated derivatives are typically nonvolatile, insoluble in organic solvents, and lacking in intense native fluorescence or other spectroscopic properties which could be exploited in analytical methods.

As part of our studies in in vivo methylation we required a sensitive and selective method of derivatization to enable the determination of 7-MeG by gas chromatography–mass spectrometry (GC–MS).[2] The results of our attempts to prepare novel derivatives of 7-MeG are summarized in this paper.

Some years ago Moschel and Leonard[3] found that 2-substituted malondialdehydes reacted with guanine to give highly fluorescent 1,N^2-prop-2-en-2-yl-1-ylideneguanine derivatives (Scheme I). We reasoned that substitution at N^7 of guanine would not dramatically affect the reaction.

Reichardt and his co-workers[4] have synthesized a large number of 2-substituted malondialdehydes that still retain their characteristic chemical reactivity, indicating that a wide range of substitution at C-2 can be tolerated. From the point of view of analytical methodology the use of a pentafluorophenyl group at C-2 would be very useful for negative ion GC–MS or electron capture detection, and we

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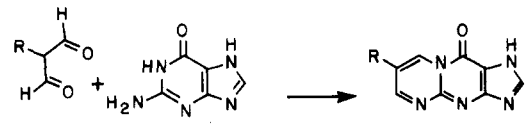
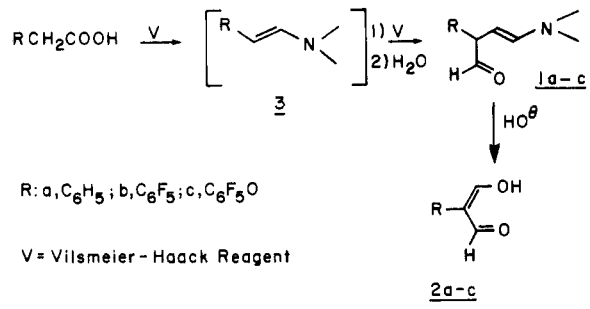
0022-3263/86/1951-3244$01.50/0

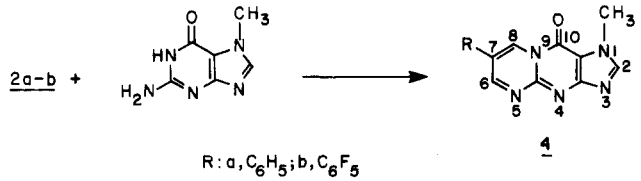
Scheme I



Scheme II



Scheme III



have undertaken the preparation and investigation of the reactions of the hitherto unreported 2-(pentafluorophenyl)- and 2-(pentafluorophenoxy)malondialdehydes.

Results and Discussion

Malondialdehyde Syntheses. Reaction of the Vilsemeier–Haack reagent[5-7] with pentafluorophenylacetic acid for 24 h afforded 2-(pentafluorophenyl)-3-(dimethylamino)acrolein (**1b**) in 36% yield (Scheme II). If shorter reaction times were used the intermediate (*E*)-β-(dimethylamino)-2,3,4,5,6-pentafluorostyrene (**3b**) could be isolated. Alkaline hydrolysis of **1b** afforded 2-(pentafluorophenyl)malondialdehyde (**2b**) in 73% yield.

The ultraviolet spectrum of **2b** showed a characteristic shift of the absorbance maximum in alkaline solution due to the acidity of the malondialdehyde moiety.

Formylation of (pentafluorophenoxy)acetic acid afforded a low yield of the corresponding 3-(dimethylamino)-2-(pentafluorophenoxy)acrolein (**1c**). Alkaline hydrolysis of **1c** gave 2-(pentafluorophenoxy)malondialdehyde (**2c**), which was identified by GC–MS in solution, but attempts to isolate the pure compound were unsuccessful due to decomposition.

Preparation and Characterization of 1,N^2-(2-R-Prop-2-en-2-yl-1-ylidene)-7-methylguanine Derivatives. 1,N^2-[2-(pentafluorophenyl)prop-2-en-2-yl-1-ylidene]-7-methylguanine (**4b**) was prepared in good yield by reaction of 7-methylguanine with excess **2b** followed by workup and flash chromatography. For comparison, 1,N^2-(2-phenylprop-2-en-2-yl-1-ylidene)-7-methylguanine (**4a**) was prepared from 7-MeG and phenylmalondialdehyde[7] (**2a**).

Both **4a** and **4b** were highly fluorescent with similar excitation and emission spectra.

4a was sufficiently volatile for GC–MS analysis to be carried out. In the GC–MS chromatograms minor unidentified products eluted well before **4b** as did unreacted **2b**. In contrast, we were unable to obtain a chromatographic peak for **4a**, which is consistent with its lack of volatility compared to **4b**.

Both derivatives gave mass spectra (electron impact, 70 eV) with base peaks corresponding to the molecular ions with little fragmentation.[8] In particular the lack of fragmentation for **4b** together with its GC properties indicate that it is a suitable derivative for quantitative determination of 7-MeG by GC–MS with selected ion monitoring.

In principle this method could be applied to other 7-alkylguanines.

Experimental Section

General Procedures. Melting points were taken on either a Mel-Temp apparatus or a Mettler hot stage apparatus and were uncorrected. Infrared spectra were measured in solvents as indicated or as KBr disks. Proton NMR spectra were measured on either a Varian T60 or a Jeol FX90Q instrument; carbon NMR spectra were measured on a Bruker WM270 instrument in solvents as indicated and with Me_4Si as reference. Mass spectra and combined gas chromatography–mass spectrometric (GC–MS) analyses were obtained on either a Hewlett-Packard 5996 or a VG Analytical 70/70 system. GC–MS analyses were carried out on the HP 5996 system using a fused silica capillary column coated with SPB-1. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN, or Elemental Microanalysis Ltd., Okehampton, U.K.

2-(Pentafluorophenyl)-3-(dimethylamino)acrolein (1b) and (*E*)-β-(Dimethylamino)-2,3,4,5,6-pentafluorostyrene (3b). Dry *N,N*-dimethylformamide (DMF, 1.85 mL, 24 mmol) was added to phosphorus oxychloride (1.85 mL, 20 mmol) under N_2 with cooling so that the temperature remained below 30 °C. Upon completion of the addition the mixture was stirred for a further 10 min. Pentafluorophenylacetic acid (1.5 g, 6.63 mmol) in DMF (2 mL) was added in one portion, and the resulting solution was stirred for 24 h at 70 °C. After cooling, the mixture was poured into ice (30 g) and neutralized with solid potassium carbonate. Potassium hydroxide (50% w/v, ca. 8 mL) was then added until gas evolution ceased (ca. 20 min). The alkaline solution was extracted with ether (4 × 50 mL), and the combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to give an oil. DMF and traces of **3b** were removed in vacuo at 60 °C and 0.1 mmHg. The brown oil was filtered through a short column of silica gel and washed with methylene chloride. After removal of the solvent in vacuo recrystallization from hexane/ethyl acetate (3:1, v/v) afforded **1b** (650 mg, 36%) as white needles: mp 115 °C; ^{1}H NMR ($CDCl_3$) δ 2.93 (s, 6 H, $N(CH_3)_2$), 7.23 (s, 1 H, =CH), 9.13 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$) 38.46 (br s, NCH_3), 45.87 (br s, NCH_3), 98.66 (s, $CHOC{=}CN(CH_3)_2$), 135.52 (s), 139.21 (s), 142.92 (s), 146.52 (s), 159.29 (d, $CHN(CH_3)_2$), 186.61 (d, CHO) ppm; ^{19}F NMR (CD_3CN) 138.84 (m, 2 F, *o*-F), 157.56 (m, 1 F, *p*-F), 164.62 (m, 2 F, *m*-F) ppm;[8,9] MS (70 eV), *m/z* (relative intensity) 266 (M + 1, 12), 265 (M, 100), 264 (10), 250 (17), 249 (11), 248 (88), 246 (29), 245 (37), 244 (71), 233 (27), 221 (38), 216 (55), 207 (21), 206 (54), 202 (19), 193 (11), 192 (17), 181 (33), 180 (10), 179 (20), 175 (10), 161 (29), 143 (27), 142 (18), 124 (11), 123 (39), 117 (13), 99 (14), 93 (18), 69 (15); IR ($CHCl_3$) 1615 cm^{-1}; UV (MeOH) λ_{max} 283 nm (ε 33 644). Anal. Calcd for $C_{11}H_8F_5NO$: C, 49.82; H, 3.04; F, 35.82. Found: C, 49.94; H, 3.05; F, 35.63.

In a separate experiment aliquots were taken from the reaction mixture at various times and worked up as described above. The ether extracts were analyzed by GC–MS to give the following results for **3b**/**1b** (h): 19 (2); 6.1 (4); 2.3 (6); 0.6 (8); 0.06 (24).

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(8) The spectra were measured on a Bruker WM250 instrument in CD_3CN and with $CFCl_3$ as reference. These ^{19}F NMR spectra represent theoretically an AA'XX'P spin system. The resolution of the spectra was insufficient for an accurate determination of the coupling constants. With the help of known absorbances of pentafluorophenyl-substituted benzene rings[9] and the coupling pattern, the signals could be assigned. The ortho, meta, and para fluorines show four, six, and three lines.
(9) Lawrenson, I. J. *J. Chem. Soc.* **1965**, 1117. Bruce, M. I. *J. Chem. Soc. A* **1968**, 1459. Bladon, P.; Sharp, D. W. A.; Winfield, J. M. *Spectrochim. Acta* **1964**, *20*, 1033.

(*E*)-β-(Dimethylamino)-2,3,4,5,6-pentafluorostyrene[10] (**3b**) was isolated by distillation [60 °C (0.1 mmHg)] to give air- and temperature-sensitive white crystals: MS, *m/z* (relative intensity) 237 (M^+, 100), 236 (12), 222 (18), 218 (35); IR ($CHCl_3$) ν 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.93 (s, 6 H, $N(CH_3)_2$), 4.85 (d, 1 H, J = 14.4 Hz, CHN), 7.25 (d, 1 H, J = 14.4 Hz, C*H*=CHN); UV (MeOH) λ_{max} 224 nm (ε 4352), 311 (25 562).

2-(Pentafluorophenoxy)-3-(dimethylamino)acrolein (1c). The Vilsmeier–Haack reagent was prepared as described above from dry DMF (4 mL, 51 mmol) and phosphorus oxychloride (4 mL, 42 mmol) and treated with pentafluorophenoxyacetic acid (3.4 g, 14 mmol) in DMF (3.5 mL). The resulting solution was stirred for 24 h at 70 °C. After cooling, the mixture was subjected to alkaline workup and extraction with ether. Flash chromatography (hexane/ethyl acetate, 1:1 v/v) afforded 720 mg (18.3%) of slightly yellow crystals. Recrystallization from hexane/ethyl acetate (10:1 v/v) gave 630 mg (16%) of white needles of **1c**: mp 82–84 °C; ^1H NMR ($CDCl_3$) δ 3.18 (s, 6 H, $N(CH_3)_2$), 6.40 (s, 1 H, =C*H*$N(CH_3)_2$), 8.70 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$) 42.92 (br s, $N(CH_3)_2$), 132.29 (s), 134.83 (s), 135.66 (s), 138.82 (s), 142.47 (s), 146.86 (d, =*C*H$N(CH_3)_2$), 179.54 (d, CHO) ppm; ^{19}F NMR (CD_3CN) 158.48 (m, 2 F, *o*-F), 166.28 (m, 2 F, *m*-F), 166.89 (m, 1 F, *p*-F) ppm;[8] MS (70 eV), *m/z* (relative intensity) 282 (M + 1, 12), 281 (M^+, 100), 252 (46), 232 (15), 224 (11), 195 (20), 181 (25), 117 (33); 114 (23), 98 (22), 86 (47), 58 (39); IR ($CHCl_3$) 1610 cm^{-1}; UV (CH_3OH) λ_{max} 298 nm (ε 35 763). Anal. Calcd for $C_{11}H_8F_5NO_2$: C, 46.99; H, 2.87; F, 33.78. Found: C, 47.05; H, 3.00; F, 33.96.

Subsequent extraction of the aqueous residue at pH 2 resulted in recovery of unreacted starting material (50%).

2-(Pentafluorophenyl)malondialdehyde (2b). A solution of **1b** (126 mg, 0.48 mmol) in 1 M sodium hydroxide (3 mL) and ethanol (2 mL) was refluxed for 1 h. After evaporation of the ethanol in vacuo the aqueous phase was diluted with water (10 mL) and extracted with ethyl acetate (3 × 10 mL) at pH 8 and then at pH 2. The combined acidic extracts were dried ($MgSO_4$) and concentrated to give **2b** (83 mg, 73%) as white crystals, mp 132–4 °C; ^1H NMR ($CDCl_3$) δ 7.33 (br s, 1 H, OH), 9.00 (s, 2 H); ^{13}C NMR (CD_3CN) 110.51 (s, CH=*C*CHO), 136.56 (s), 140.16 (s), 143.47 (s), 147.16 (s), 179.26 (d, HO*C*H=*C*CHO) ppm; ^{19}F NMR (CD_3CN) 138.27 (m, 2 H, *o*-F), 155 (m, 1 H, *p*-F), 163.74 (m, 2 H, *m*-F) ppm;[8] MS (70 eV), *m/z* (relative intensity) 239 (M^+ + 1, 8), 238 (M^+, 76), 209 (18), 192 (86), 181 (67), 163 (17), 162 (34), 161 (100), 143 (22), 142 (19), 141 (12), 132 (12), 130 (12), 123 (21), 117 (11), 111 (10), 99 (11), 93 (20), 75 (11); IR (CH_3CN) 3800–3300, 1630 cm^{-1}; UV: (MeOH) λ_{max} 255 nm (ε 17 863), (0.1 N HCl) 248 (19 289), 0.1 N NaOH) 266 (29 603). Anal. Calcd for $C_8H_3F_5O_2$: C, 45.39; H, 1.27; F, 39.89. Found: C, 45.14; H, 1.28; F, 40.08.

2-(Pentafluorophenoxy)malondialdehyde (2c). **1c** was hydrolyzed under alkaline conditions and extracted as for **1**. Evaporation of the organic solvent at room temperature resulted in decomposition of the product, which was identified in solution by GC–MS (70 eV) *m/z* (relative intensity) 254 (M^+, 67) 197 (33) 184 (44) 168 (24) 167 (16) 155 (26) 136 (48) 119 (11) 117 (55) 105 (10) 99 (14) 98 (13) 93 (17) 69 (18) 58 (100).

7-(Pentafluorophenyl)-10-oxo-1-methyl-9,10-dihydropyrimido[1,2-*a*]purine or 1,N^2-[2-(Pentafluorophenyl)-prop-2-en-2-yl-1-ylidene]-7-methylguanine (4b). 7-Methylguanine (33 mg, 0.2 mmol) and **2b** (200 mg, 0.83 mmol) in glacial acetic acid (7 mL) were heated under reflux under N_2 for 12 h. Evaporation of the solvent afforded a yellow residue, which was dissolved in methylene chloride (25 mL) and was washed with cold solutions of sodium bicarbonate (saturated), potassium dihydrogen phosphate (0.1 M, pH 7), and water. The organic phase was then poured directly into the top of a small flash chromatography column. The fluorescent product was eluted to the middle of the column with acetonitrile, and then the eluant was changed to dry tetrahydrofuran. The pooled fluorescent fractions were evaporated to yield **4b** (64 mg, 87%) as bright yellow crystals: mp 300 °C dec; ^1H NMR (CD_3CO_2D) δ 4.17 (s, 3 H, CH_3), 8.37 (s, 1 H, H_2), 9.04 (m, 1 H, H_8 or H_6); 9.44 (m, 1 H, H_6 or H_8); ^{13}C NMR (CD_3COOD) 34.79 (d), 111.72 (s), 137.45 (s), 138.48 (d), 141.15 (s), 144.08 (s), 144.68 (s), 147.75 (s), 148.68 (s), 149.34 (d), 151.21 (s), 157.38 (s), 161.96 (d) ppm; MS (70 eV); *m/z* (relative intensity) 367 (M^+, 100), 348 (17), 311 (10), 271 (13), 245 (22), 192 (19), 165 (13), 147 (11), 93 (20), 67 (19), 53 (20); UV (CH_3CN) λ_{max} 233 nm (ε 24 676), 269 (24 561), 330 (5747); fluorescence spectrum (CH_3CN), λ_{max} (excitation) 280, 340, (emission) 500 nm. Anal. Calcd for $C_{15}H_6F_5N_5O$: C, 49.06; H, 1.65; N, 19.07; F, 25.87. Found: C, 49.25; H, 1.68; N, 18.95; F, 25.56. GC–MS analysis: column, Supelco SPB-1 20 m × 0.2 mm i.d., 0.25-μm coat thickness; carrier gas, helium at 45 kPa; temperature program, 60 °C for 0.5 min and then to 300 °C at 30 °C/min; retention time of **4b**, 10.47 min.

7-Phenyl-10-oxo-1-methyl-9,10-dihydropyrimido[1,2-*a*]-purine or 1,N^2-(2-Phenylprop-2-en-2-yl-1-ylidene)-7-methylguanine (4a). 7-Methylguanine (50 mg, 0.3 mmol) and phenylmalondialdehyde[6] (**1a**, 89.6 mg, 0.6 mmol) in 50% aqueous acetic acid (4 mL) was heated in a screw-top test tube at 140 °C for 16 h. Upon cooling in the refrigerator for 3 days crystals of pure **4a** separated out, which were filtered, washed with water, and dried in vacuo over P_2O_5: mp 274–275 °C; yield, 35 mg (42%); ^1H NMR (Me_2SO-d_6) δ 4.11 (s, 3 H, NCH_3), 7.53–7.95 (m, 5 H, Ar), 8.49 (s, 1 H, CH), 9.34 (d, 1 H, J = 3.4 Hz, CH), 9.44 (d, 1 H, J = 3.4 Hz, CH); MS (70 eV) *m/z* (relative intensity) 277 (M^+, 100), 276 (43), 248 (6), 221 (7), 181 (11), 155 (11), 102 (18), 93 (11), 77 (10); UV (CH_3CN) 240 nm (ε 30 600), 274 (27 900), 326 (6420), 377 (sh, 2565); fluorescence spectrum (CH_3CN), λ_{max} (excitation) 294, 340, (emission) 504 nm). Anal. Calcd for $C_{15}H_{11}N_5O$: C, 65.00; H, 3.97; N, 25.30. Found: C, 65.28; H, 4.18; N, 25.12.

Acknowledgment. This investigation was supported by PHS Grant PO1-ES00597, awarded by the National Institute of Environmental Health Sciences, DHHS.

Registry No. **1a**, 103025-45-2; **1b**, 103025-40-7; **1c**, 103025-41-8; **2b**, 103025-42-9; **2c**, 103190-47-2; **3b**, 103067-97-6; **4a**, 103025-44-1; **4b**, 103025-43-0; (pentafluorophenoxy)acetic acid, 14892-14-9; (pentafluorophenyl)acetic acid, 653-21-4; 7-methylguanine, 578-76-7.

(10) The *E* configuration is assigned on the basis of the large coupling constant.